Brigham and Women's Hospital
Founding Member, Mass General Brigham

PNEUMONIA: Community and Hospital Acquired, Including a Case Study

Rebecca M. Baron, MD
Associate Physician
Division of Pulmonary and Critical Care Medicine
Brigham and Women's Hospital
Associate Professor of Medicine
Harvard Medical School

CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE

BWH BRIGHAM AND WOMEN'S HOSPITAL
The Lung Center

HARVARD MEDICAL SCHOOL
TEACHING HOSPITAL

Rebecca M. Baron, M.D.

Harvard Medical School

Residency: BWH

Pulmonary/Critical Care Fellowship: Harvard Combined Program

ICU attending

Translational investigator: Sepsis, ARDS, Lung Injury

Disclosures

- None

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY MAY 2019 AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA AUGUST 2019

October 1, 2019

Please note (though I won't discuss in detail today):

COVID

Table 2. Differences between the 2019 and 2007 American Thoracic Society/Infectious Diseases Society of America Community-acquired Pneumonia Guidelines

Recommendation	2007 ATS/IDSA Guideline	2019 ATS/IDSA Guideline
Sputum culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *Pseudomonas aeruginosa*
Blood culture	Primarily recommended in patients with severe disease	Now recommended in patients with severe disease as well as in all inpatients empirically treated for MRSA or *P. aeruginosa*
Macrolide monotherapy	Strong recommendation for outpatients	Conditional recommendation for outpatients based on resistance levels
Use of procalcitonin	Not covered	Not recommended to determine need for initial antibacterial therapy
Use of corticosteroids	Not covered ****	Recommended not to use. May be considered in patients with refractory septic shock
Use of healthcare-associated pneumonia category	Accepted as introduced in the 2005 ATS/IDSA hospital-acquired and ventilator-associated pneumonia guidelines	Recommend abandoning this categorization. Emphasis on local epidemiology and validated risk factors to determine need for MRSA or *P. aeruginosa* coverage. Increased emphasis on deescalation of treatment if cultures are negative
Standard empiric therapy for severe CAP	β-Lactam/macrolide and β-lactam/fluoroquinolone combinations given equal weighting	Both accepted but stronger evidence in favor of β-lactam/macrolide combination
Routine use of follow-up chest imaging	Not addressed	Recommended not to obtain. Patients may be eligible for lung cancer screening, which should be performed as clinically indicated

Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*.

Reaction to the Guidelines

"Welcomed recommendations:"

- Abandonment of HCAP
- More restrictive indication for empiric macrolides in outpatients
- Increased emphasis on microbiology diagnostics
- Addressing corticosteroid use

"Critiques of recommendations:"

- "Somewhat arbitrary choice of a 25% resistance threshold for outpatient macrolide monotherapy. Experts from areas with elevated mycobacterial prevalence particularly opposed the recommendation of fluoroquinolones, even as an alternative."

"International perspective on the new 2019 ATS/IDSA CAP guideline – a critical appraisal by a global expert panel Authors" ; Chest 2020 (Aug 25)

Additional interim data since 2019

- More support for macrolide preference
- Hydrocortisone (low dose) beneficial for severe pneumonia (that we'll discuss)
- Of note, majority of published data recently relates to COVID rather than non-COVID pneumonia.

(1) Crit Care 2023;27(1):212
(2) NEJM 2023;388(21):1931.

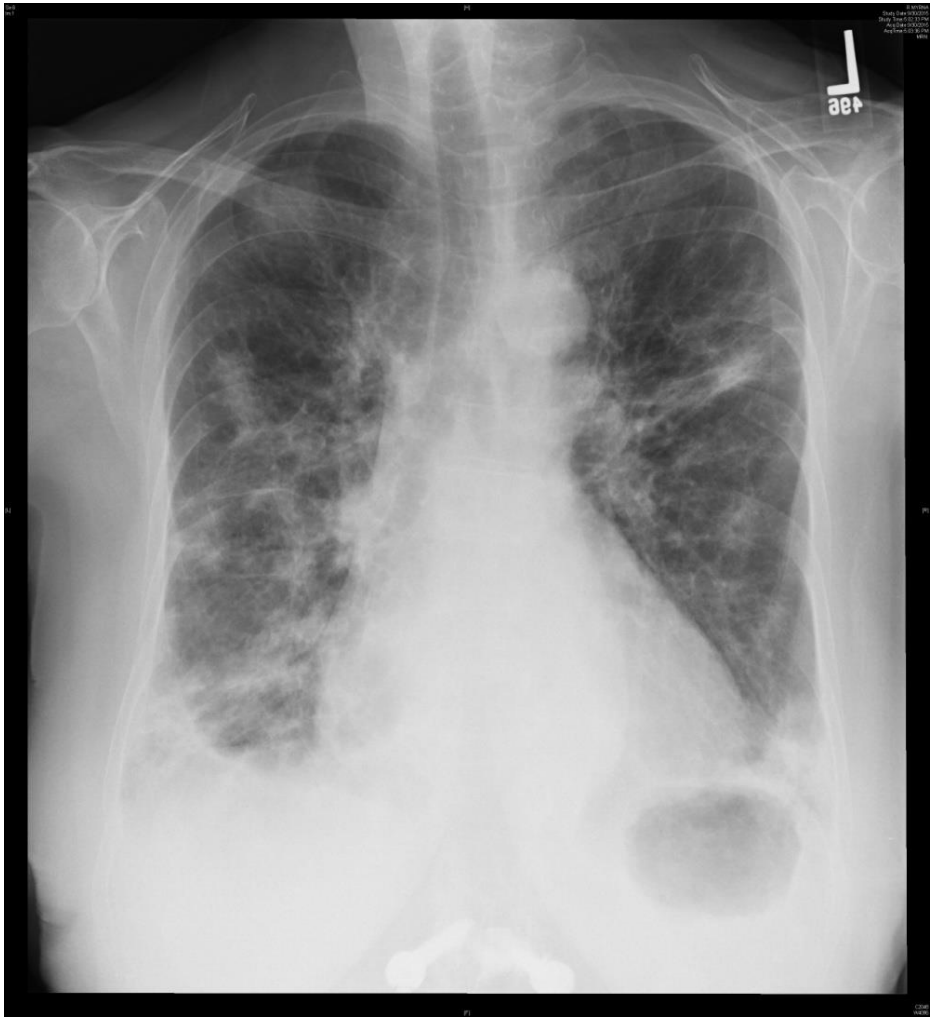
The Case

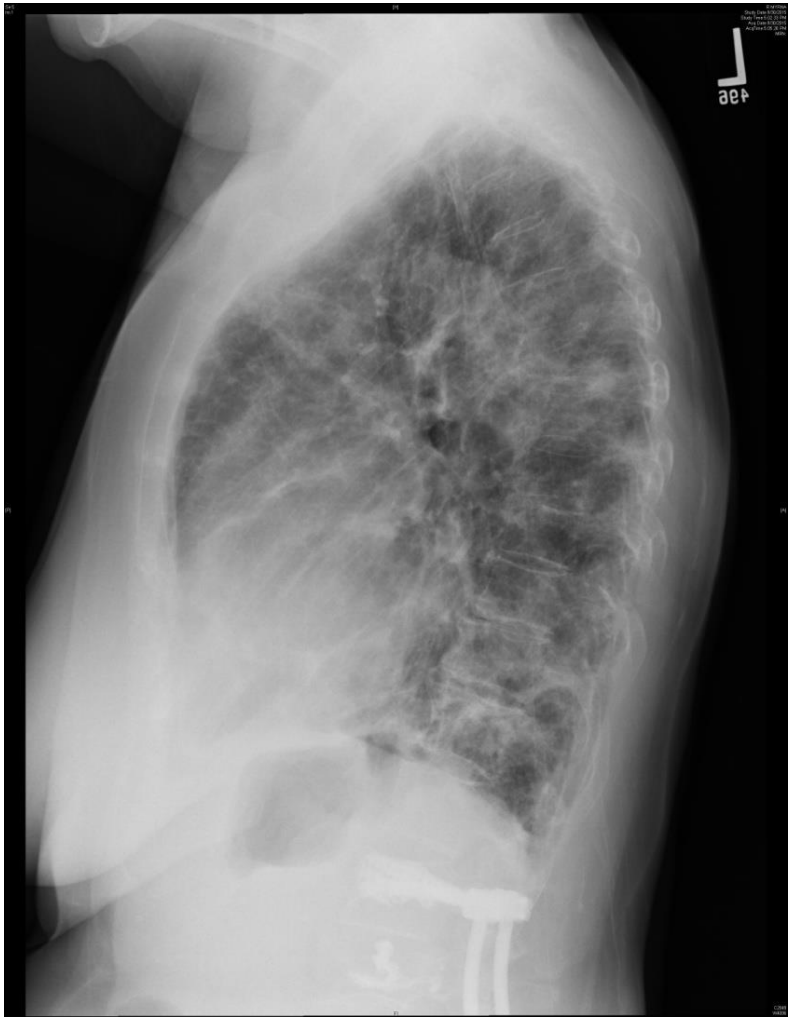
- 83 yo woman presents to outpatient clinic with report of fevers, chills, SOB, cough
- PMH/meds:
  - Atrial fibrillation on Coumadin
  - Asthma
  - Neurogenic bladder previously on nitrofurantoin
  - Recent E. Coli UTI/bacteremia (at OSH)

Case, continued, outpatient setting

- Exam:
  - 93% Room Air
  - Temp 98°F, 125/80, HR 80 irregularly irregular
  - Coarse BS with crackles R>L lower lobes, no murmurs nor RV heave, no lower extremity edema nor clubbing

First CXR





What would you do?

COMMUNITY ACQUIRED PNEUMONIA (CAP)

- Infection of the lung parenchyma in a person who is not hospitalized or living in a long-term facility for ≥ 2 weeks.

Niederman, et al. Clin Therapeutics, 1998;20; 820-837.

http://www.lungusa.org/site

CAP--Epidemiology

- Leading infectious cause of death in US
- 4.8 million cases per year in the USA
- 1.3 million hospitalizations per year
- 80,000 deaths per year
  - Outpatient 1-2%
  - Inpatient 10-14%
  - ICU 40%

MECHANISM OF INFECTION

- **Air borne** – via the tracheobronchial tree (infected bronchoscope, aspiration or inhalation of micro-organisms) or extension into airway from parenchyma*
- Hematogenous
- Direct spread from mediastinum, diaphragm or chest wall

*What if there's a lung microbiome that's dysregulated? – 2018 data suggests might be.

Etiology of CAP (%)

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
M. pneumonia	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

OP=Outpatient, IP=Inpatient

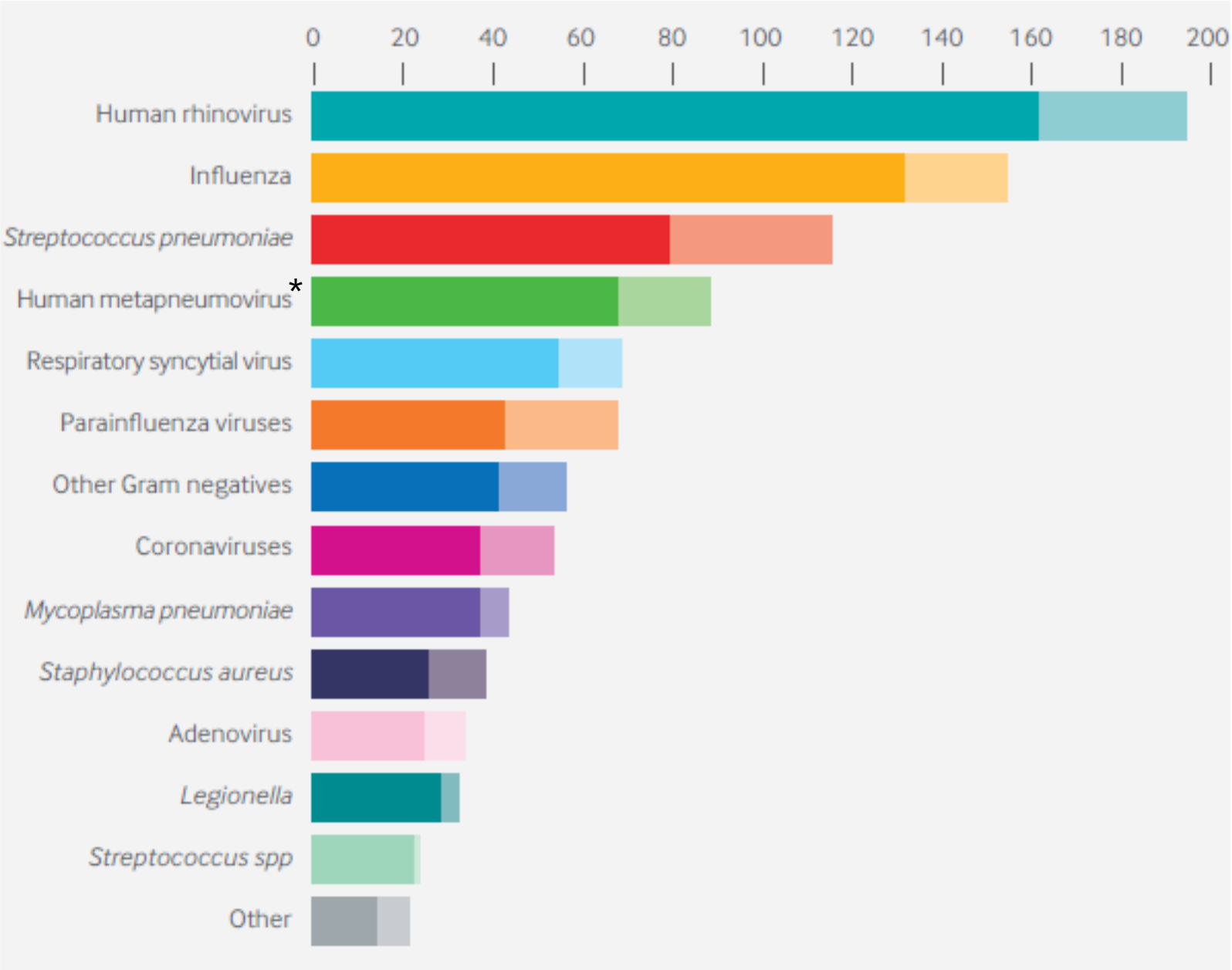


Fig 3| Pathogens detected in patients with radiographic community acquired pneumonia from the Centers for Disease Control EPIC study. Lighter bars indicate co-detections of more than one pathogen. From Jain et al[19] NEJM 2015

Clinical Diagnosis, Triad:

- Signs of infection (Fever, leukocytosis)
- Respiratory symptoms (cough, shortness of breath, sputum, chest pain, abnormal pulmonary examination)
- New or changed infiltrate on Chest X-Ray

N Engl J Med 2014; 370;6

Clinical Diagnosis

- With rhinorrhea or sore throat, think of another diagnosis.*

- Elderly patients: may have few or no respiratory symptoms (e.g. confusion or abdominal pain).

- Diagnosis may be complicated in patients with underlying lung disease or lung disease processes (e.g., CHF)

*note COVID

Clinical Diagnosis

- "Atypical pneumonia":
  - gradual onset
  - lacks mucoid sputum production
  - often associated with extrapulmonary symptoms/signs

- **Clinicians often cannot accurately distinguish "typical" from "atypical" pneumonia on clinical grounds**

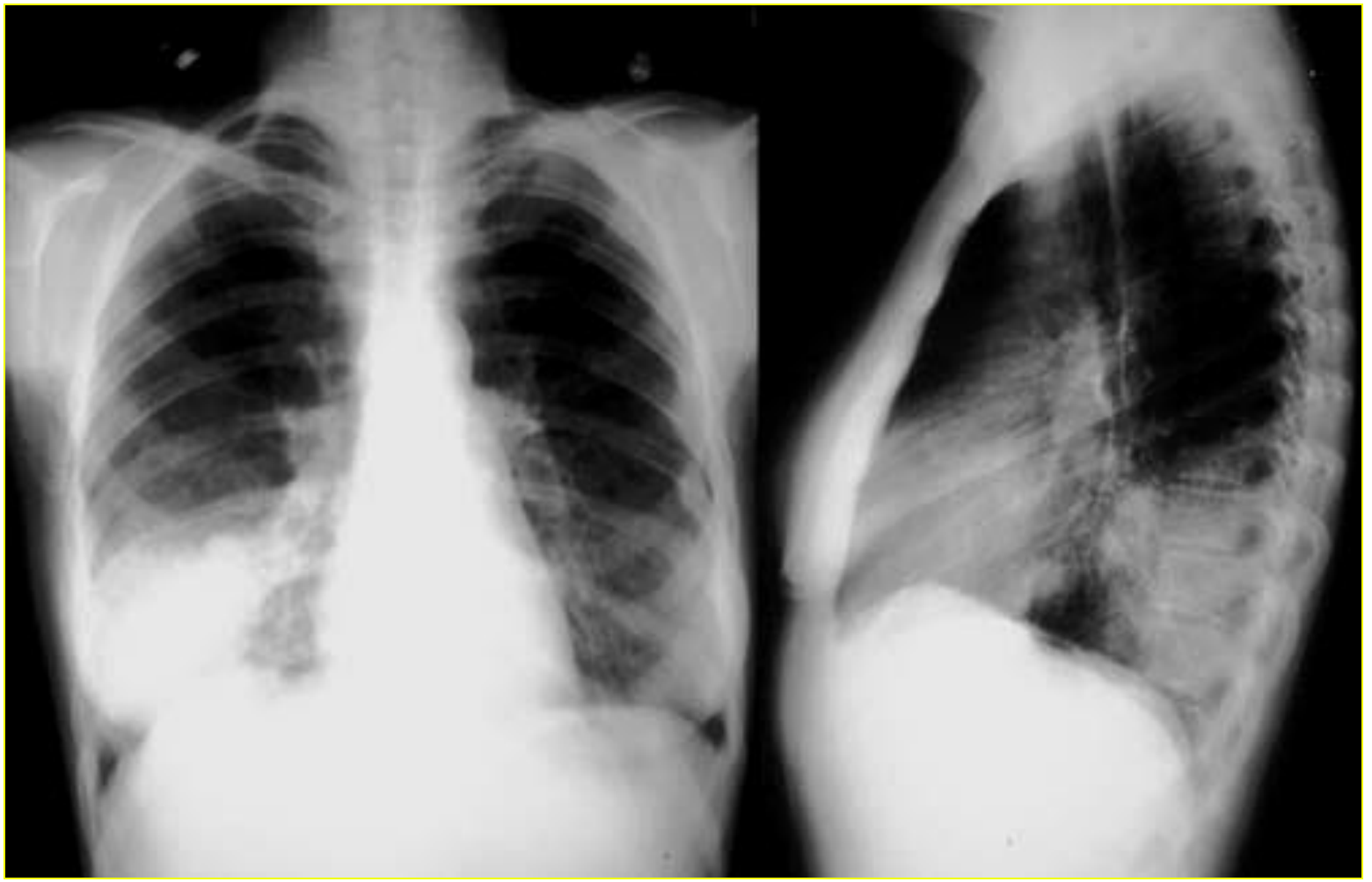
Chest Radiograph

- IDSA guidelines:

> In addition to a constellation of suggestive clinical features, a demonstrable infiltrate by chest radiograph or other imaging technique, with or without supporting microbiological data, is required for the diagnosis of pneumonia. (Moderate recommendation; level III evidence.)

- Infiltrates may be subtle—radiologists may miss 15% of infiltrates and disagreement amongst radiologists reported 10% of the time.

Chest Radiograph



Chest Radiograph

- Assessing response to therapy:
  - Tobacco smokers or those 65 years old should get a follow-up CXR in 3-6 months.
  - Age <50 usually clear 3-4 weeks
  - Age >50 usually clear by 8-12 weeks
- However…

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 16: For CAP that is improving is a f/u CXR needed?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 16: For CAP that is improving is a f/u CXR needed?

No, if improved within 5-7d. Value was for detecting new malignancy, but data suggests most of those were smokers who would meet lung cancer screening criteria.

ROLE OF CT*

- Adjunct to CXR, especially in immune-compromised hosts or atypical findings
- Recent studies show discrepancy with 'overcalls' on CXR when compared with CT
- Superior in detecting:
  - airspace disease
  - centrilobular and acinar nodules
  - centrilobular or perilobular distribution
  - ground glass opacities
  - air bronchograms

*Increasing interest in u/s

Other testing, routinely?

- Optional for outpatients
- Additional testing suggested if result would change antibiotic therapy and/or if thought be high yield especially in those likely to have resistant organisms
- Critically ill patients require additional diagnostics
- Influenza testing during appropriate season*

*note COVID

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Questions 1-2: In Adults with CAP, Should Gram Stain and Culture of Lower Respiratory Secretions and BCXs Be Obtained at the Time of Diagnosis?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Questions 1-2: In Adults with CAP, Should Gram Stain and Culture of Lower Respiratory Secretions and BCXs Be Obtained at the Time of Diagnosis?

Outpatient: no

Inpatient: Yes. for severe CAP (post intubation secretions better yield diagnostically), empiric MRSA/pseudomonas coverage, hx MRSA/pseudomonas, hospitalization/abx within 90d (left to discretion of clinical/setting for other inpatients)

Unclear data that cultures beneficial; obtaining reliable cultures is difficult

Research needs: rapid diagnostics

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 3: In Adults with CAP, Should Legionella and Pneumococcal Urinary Antigen Testing Be Performed at the Time of Diagnosis?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 3: In Adults with CAP, Should Legionella and Pneumococcal Urinary Antigen Testing Be Performed at the Time of Diagnosis?

Not routinely, unless recent outbreak/epidemiologic rationale, or severe CAP (data hasn't borne out for testing with less severe disease and concern for narrowing treatment prematurely with pos testing) – Yes for severe CAP: Legionella UAg and lower resp tract secretions for cx or NAAT

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 4: In adults with CAP should a respiratory sample for influenza be sent at the time of diagnosis?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 4: In adults with CAP should a respiratory sample for influenza be sent at the time of diagnosis?

Yes advised for molecular test rather than Ag test during flu season

Clinical Indications for More Extensive Diagnostic Testing

Indication	Blood culture	Sputum culture	*Legionella* UAT	Pneumococcal UAT	Other
Intensive care unit admission	X	X	X	X	X[a]
Failure of outpatient antibiotic therapy		X	X	X	
Cavitary infiltrates	X	X			X[b]
Leukopenia	X			X	
Active alcohol abuse	X	X	X	X	
Chronic severe liver disease	X			X	
Severe obstructive/structural lung disease		X			
Asplenia (anatomic or functional)	X			X	
Recent travel (within past 2 weeks)			X		X[c]
Positive *Legionella* UAT result		X[d]	NA		
Positive pneumococcal UAT result	X	X		NA	
Pleural effusion	X	X	X	X	X[e]

NOTE. NA, not applicable; UAT, urinary antigen test.

[a] Endotracheal aspirate if intubated, possibly bronchoscopy or nonbronchoscopic bronchoalveolar lavage.
[b] Fungal and tuberculosis cultures.
[c] See table 8 for details.
[d] Special media for *Legionella*.
[e] Thoracentesis and pleural fluid cultures.

IDSA Guidelines, 2007

JAMA Network Open

March 6, 2024

Original Investigation | Infectious Diseases

Diagnostic Stewardship in Community-Acquired Pneumonia With Syndromic Molecular Testing

A Randomized Clinical Trial

Dagfinn L. Markussen, MD; Sondre Serigstad, MD, PhD; Christian Ritz, PhD; Siri T. Knoop, MD, PhD; Marit H. Ebbesen, MD, PhD; Daniel Faurholt-Jepsen, MD, PhD; Lars Heggelund, MD, PhD; Cornelis H. van Werkhoven, MD, PhD; Tristan W. Clark, MD; Rune O. Bjørneklett, MD, PhD; Øyvind Kommedal, MD, PhD; Elling Ulvestad, MD, PhD; Harleen M. S. Grewal, MD, PhD

- Single center: 374 ED CAP pts randomized to Biofire PCR vs. Microbial culture in single center in Norway.
- Molecular testing increased pathogen-specific treatment and reduced time to pathogen specific treatment by 9.4 hours
- Increasing use of PCR testing in some institutions.
- Likely more molecular testing on the horizon.

Blood Cultures

- 13% sensitivity
- Track *S.pneumoniae* antimicrobial sensitivity
- Marker for high risk

Gram Stain & Sputum Culture

- 30% pneumonia, non-productive
- 14% adequate sputum sample G.S.
- 15-30% prior antibiotic therapy
- 40-60% “negative” culture results

→Etiology can be established <50% of cases, and
→Etiologic dx does NOT reduce mortality, LOS, cost
→Testing can potentially delay treatment

Clin Inf Dis. 2001;32:701-707; Archives Int Med. 2004;164:1907-11;
Clin Inf Dis. 1998; 26:811; Sem in Resp Infect. 1997; 12:308.

Risk Stratification in CAP

- Many prediction models available
- Large retrospective and prospective cohorts demonstrate that medical co-morbidities, age, physical exam findings and laboratory results can predict mortality
- Goal of prediction rules is to identify *low-risk patients who may not need hospitalization.*

Risk Stratification in CAP

- CURB-65 (easier system, less well validated)
- Pneumonia Severity Index (PSI)
- IDSA Recommendations:

> Objective criteria or scores should always be supplemented with physician determination of subjective factors, including the ability to safely and reliably take oral medication and the availability of outpatient support resources. (Strong recommendation; level II evidence.)

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 6: Should a clinical prediction rule used to help guide inpatient or outpatient PNA treatment?

Question 7: Should a clinical prediction rule used to help guide location of treatment within the hospital setting?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 6: Should a clinical prediction rule used to help guide inpatient or outpatient PNA treatment?

Recommend PSI over CURB-65 – PSI better discrimination and predictability for safe outpatient treatment (though may underestimate illness severity in younger patients)

Question 7: Should a clinical prediction rule used to help guide location of treatment within the hospital setting?

Suggest using major vs. minor severity criteria. PSI and CURB-65 not validated for this purpose. Worse outcomes with initial mis-triage.

Criteria for Severe CAP

Minor criteria[a]

- Respiratory rate[b] ≥30 breaths/min
- PaO_2/FiO_2 ratio[b] ≤250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (BUN level, ≥20 mg/dL)
- Leukopenia[c] (WBC count, <4000 cells/mm^3)
- Thrombocytopenia (platelet count, <100,000 cells/mm^3)
- Hypothermia (core temperature, <36°C)
- Hypotension requiring aggressive fluid resuscitation

Major criteria

- Invasive mechanical ventilation
- Septic shock with the need for vasopressors

NOTE. BUN, blood urea nitrogen; PaO_2/FiO_2, arterial oxygen pressure/fraction of inspired oxygen; WBC, white blood cell.

[a] Other criteria to consider include hypoglycemia (in nondiabetic patients), acute alcoholism/alcoholic withdrawal, hyponatremia, unexplained metabolic acidosis or elevated lactate level, cirrhosis, and asplenia.

[b] A need for noninvasive ventilation can substitute for a respiratory rate >30 breaths/min or a PaO_2/FiO_2 ratio <250.

[c] As a result of infection alone.

CID 2007

Etiology of CAP (%)

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
M. pneumonia	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

Beta-lactam activity

Etiology of CAP (%)

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
M. pneumonia	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

Macrolide activity

Etiology of CAP (%)

So-so

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
*M. pneumonia**	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

*Increasing resistance reported.

Atypical coverage particularly important for young adults (herd immunity from pneumococcal vaccine)

Tetracyclines

Etiology of CAP (%)

Okay

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
M. pneumonia	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

Fluoroquinolone activity

Etiology of CAP (%)

	OP (n=547)	IP (n=6152)	ICU (n=1415)
Unknown	64.4	48.3	39.7
S. pneumonia	4	20.3	22.5
H. influenza	4	6	5.3
M. pneumonia	15.3	3.9	1.9
C. pneumonia	4.5		
Legionella spp.	0.9	3.4	5.9
S. aureus		1.8	2.5
GNR		3.2	10
P. carinii		1.3	1.6
Influenza	3.5	2.8	
Polymicrobial	1.5	8.6	5.4

Webster et.al. AFC 2004;8;3-6

When to suspect MRSA ….

- Health care associated
- History of MRSA colonization
- Recent antibiotic exposure
- Sicker than you expect
- Not responding to standard antibiotics
- Rapid recurrence

Table 3. Clinical Features Suggesting Community-Acquired MRSA Pneumonia.*

Cavitary infiltrate or necrosis
Rapidly increasing pleural effusion -- “Dirty dishwater”
Gross hemoptysis (not just blood-streaked)
Concurrent influenza
Neutropenia
Erythematous rash
Skin pustules
Young, previously healthy patient
Severe pneumonia during summer months

* MRSA denotes methicillin-resistant *Staphylococcus aureus*.

N Engl J Med 2014; 370;6

Table 3. Initial Treatment Strategies for Outpatients with Community-acquired Pneumonia

	Standard Regimen
No comorbidities or risk factors for MRSA or *Pseudomonas aeruginosa**	Amoxicillin or doxycycline or macrolide (if local pneumococcal resistance is <25%)†
With comorbidities‡	Combination therapy with amoxicillin/clavulanate or cephalosporin AND macrolide or doxycycline§ OR monotherapy with respiratory fluoroquinolone‖

Definition of abbreviations: ER = extended release; MRSA = methicillin-resistant *Staphylococcus aureus*.

*Risk factors include prior respiratory isolation of MRSA or *P. aeruginosa* or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 d).

†Amoxicillin 1 g three times daily, doxycycline 100 mg twice daily, azithromycin 500 mg on first day then 250 mg daily, clarithromycin 500 mg twice daily, or clarithromycin ER 1,000 mg daily.

‡Comorbidities include chronic heart, lung, liver, or renal disease; diabetes mellitus; alcoholism; malignancy; or asplenia.

§Amoxicillin/clavulanate 500 mg/125 mg three times daily, amoxicillin/clavulanate 875 mg/125 mg twice daily, 2,000 mg/125 mg twice daily, cefpodoxime 200 mg twice daily, or cefuroxime 500 mg twice daily; AND azithromycin 500 mg on first day then 250 mg daily, clarithromycin 500 mg twice daily, clarithromycin ER 1,000 mg daily, or doxycycline 100 mg twice daily.

‖Levofloxacin 750 mg daily, moxifloxacin 400 mg daily, or gemifloxacin 320 mg daily.

2019

Table 4. Initial Treatment Strategies for Inpatients with Community-acquired Pneumonia by Level of Severity and Risk for Drug Resistance

	Standard Regimen	Prior Respiratory Isolation of MRSA	Prior Respiratory Isolation of *Pseudomonas aeruginosa*	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for *P. aeruginosa*
Nonsevere inpatient pneumonia*	β-Lactam + macrolide† or respiratory fluroquinolone‡	Add MRSA coverage§ and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy	Obtain cultures but withhold MRSA coverage unless culture results are positive. If rapid nasal PCR is available, withhold additional empiric therapy against MRSA if rapid testing is negative or add coverage if PCR is positive and obtain cultures	Obtain cultures but initiate coverage for *P. aeruginosa* only if culture results are positive
Severe inpatient pneumonia*	β-Lactam + macrolide† or β-lactam + fluroquinolone‡	Add MRSA coverage§ and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy	Add MRSA coverage§ and obtain nasal PCR and cultures to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy

Definition of abbreviations: ATS = American Thoracic Society; CAP = community-acquired pneumonia; HAP = hospital-acquired pneumonia; IDSA = Infectious Diseases Society of America; MRSA = methicillin-resistant *Staphylococcus aureus*; VAP = ventilator-associated pneumonia.

*As defined by 2007 ATS/IDSA CAP severity criteria guidelines (*see* Table 1).

†Ampicillin + sulbactam 1.5–3 g every 6 hours, cefotaxime 1–2 g every 8 hours, ceftriaxone 1–2 g daily, or ceftaroline 600 mg every 12 hours AND azithromycin 500 mg daily or clarithromycin 500 mg twice daily.

‡Levofloxacin 750 mg daily or moxifloxacin 400 mg daily.

§Per the 2016 ATS/IDSA HAP/VAP guidelines: vancomycin (15 mg/kg every 12 h, adjust based on levels) or linezolid (600 mg every 12 h).

‖Per the 2016 ATS/IDSA HAP/VAP guidelines: piperacillin-tazobactam (4.5 g every 6 h), cefepime (2 g every 8 h), ceftazidime (2 g every 8 h), imipenem (500 mg every 6 h), meropenem (1 g every 8 h), or aztreonam (2 g every 8 h). Does not include coverage for extended-spectrum β-lactamase–producing Enterobacteriaceae, which should be considered only on the basis of patient or local microbiological data.

ABANDON HCAP

Lancet 2024: ? Anti-inflammatory effect of added macrolide?

2021 onward: ensure appropriate (adequate) antibiotic dosing

Original Investigation | Caring for the Critically Ill Patient

June 12, 2024

Prolonged vs Intermittent Infusions of β-Lactam Antibiotics in Adults With Sepsis or Septic Shock

A Systematic Review and Meta-Analysis

Mohd H. Abdul-Aziz, BPharm, PhD[1]; Naomi E. Hammond, RN, PhD[2,3]; Stephen J. Brett, MD[4]; et al

- Prolonged β-lactam infusions were associated with lower 90d mortality in ICU sepsis and septic shock patients, vs. intermittent infusions
- Extended infusions (3-4 hours) have been considered similarly in analysis to continuous infusions
- Pharmacy consultation in our ICU has been incredibly helpful

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 10: For inpatients should suspected aspiration be treated with additional coverage for anaerobes?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 10: For inpatients should suspected aspiration be treated with additional coverage for anaerobes?

Not suggested routinely unless lung abscess or empyema suspected. Not clear in more recent studies how common anaerobic organisms are and concern for increased abx use promoting increased resistance.

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 13: For those with CAP and who test positive for influenza, should treatment be initiated?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 13: For those with CAP and who test positive for influenza, should treatment be initiated?

Yes, for inpatients and outpatients. Likely most benefit within 2d but may be benefit 4-5 days out.

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 14: For those testing positive for flu, should antibacterial therapy be given too?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 14: For those testing positive for flu, should antibacterial therapy be given too?

Yes, in- and outpatient. Co-infections are common and may be hard to specifically diagnose and/or exclude.

Tailor antibiotics once the pathogen is known ….

- *S. pneumoniae*→ penicillin (if sensitive)
- *Mycoplasma* or *Chlamydia*→ macrolide or tetracycline
- *Legionella*→ fluoroquinolone

Duration of treatment

- Mild Disease: As little as 5 days may be sufficient especially if non-immunocompromised hosts
- Moderate-Severe Disease: 7-8 days, unless non-fermenting gram-negative rods, then some data supports 15 days
- Early IV to oral, when feasible decreases cost and LOS
- Procalcitonin?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 15: What is the appropriate duration of abx for inpatient and outpatient CAP?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 15: What is the appropriate duration of abx for inpatient and outpatient CAP?

Until the patient is stable, and no less than 5d (unless more complicated additional infections like meningitis or other unusual pathogens, etc) and 7d for MRSA or pseudomonas. 2024 study in VAP (LRM) suggested noninferiority of median 6 vs 14d with fewer abx associated side effects with shorter course.

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 5: In adults with CAP should serum procalcitonin testing be used to withhold antibiotics?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

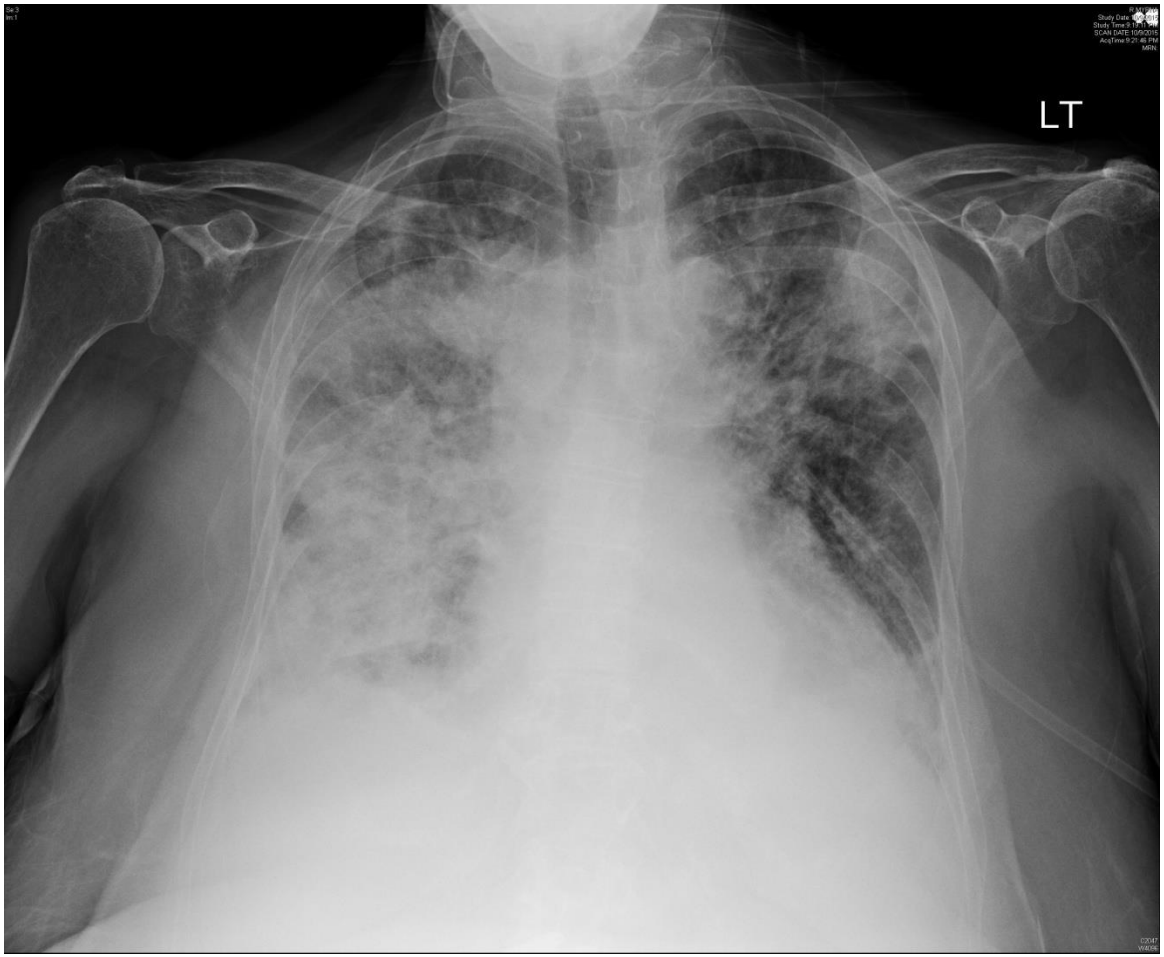
Question 5: In adults with CAP should serum procalcitonin testing be used to withhold antibiotics?

No – empiric abx recommended for clinically suspected and radiographically confirmed CAP – broad range of sensitivity for the testing and thus can't use to withhold abx. Studies have not examined using procalcitonin for guiding initiation in radiographically confirmed pneumonia.

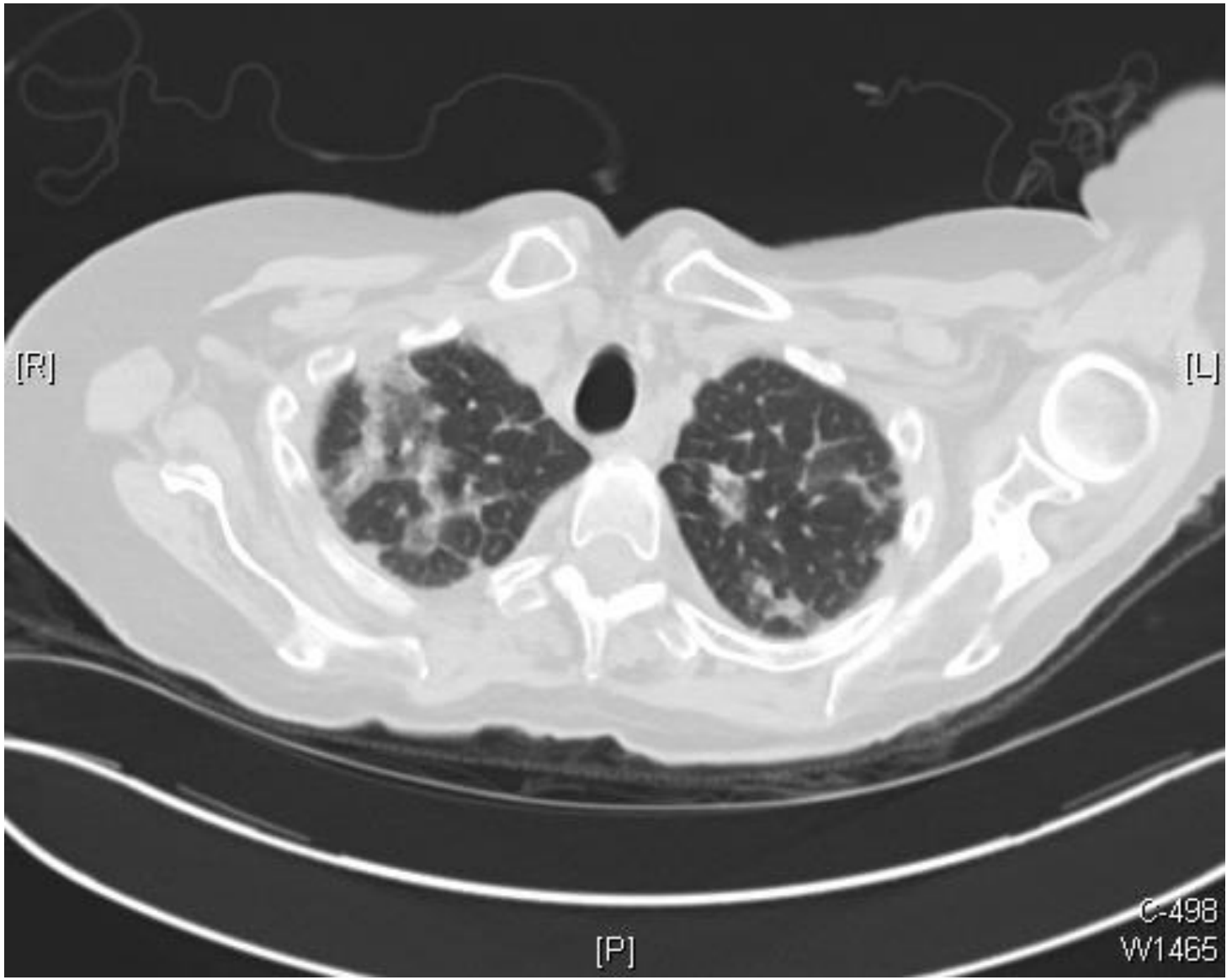
Case, continued:

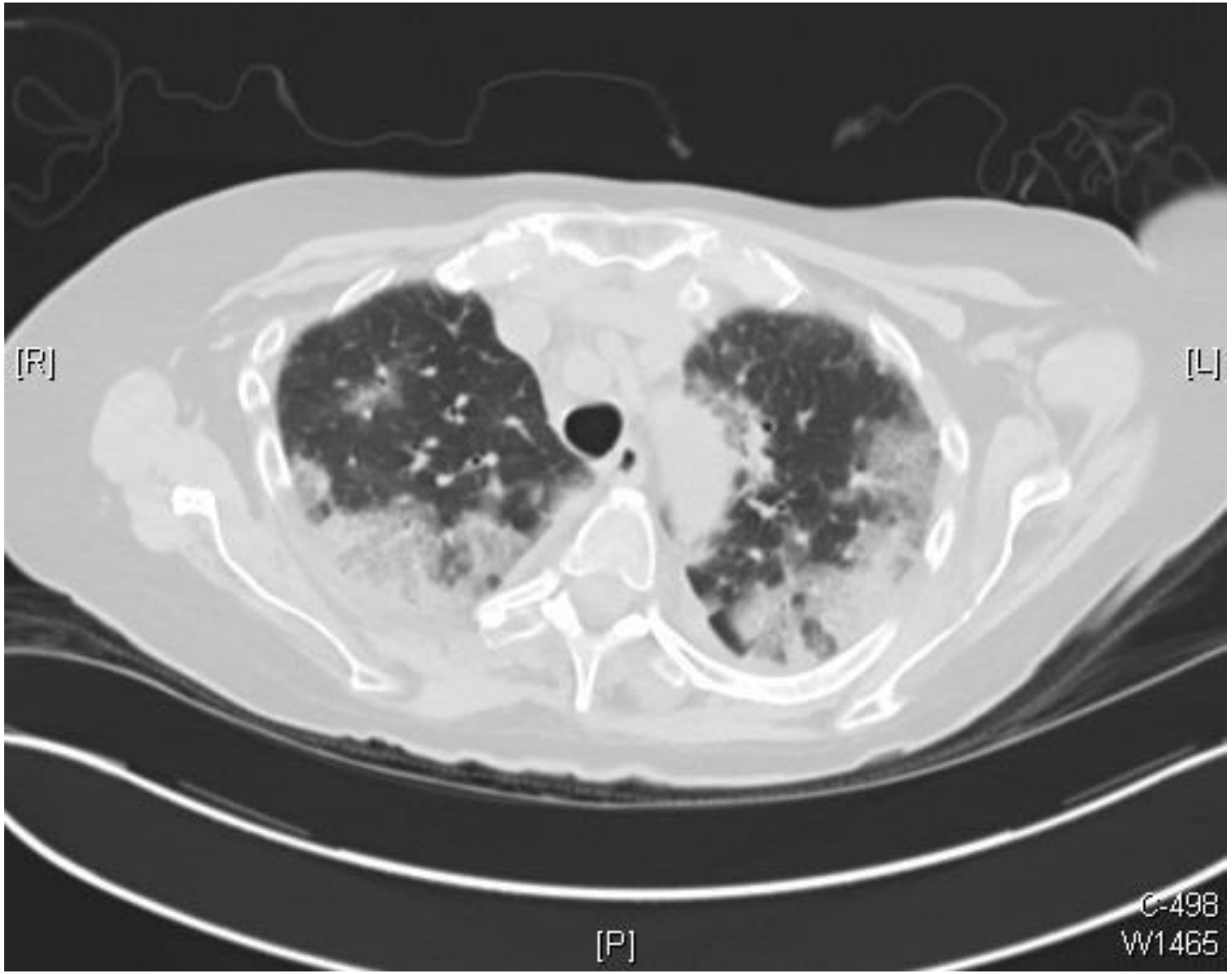
- She is given 5d of azithromycin and doxycycline
- 8 days later, she is seen in pulmonary clinic
  - T101
  - Room Air sats 80s, dyspneic

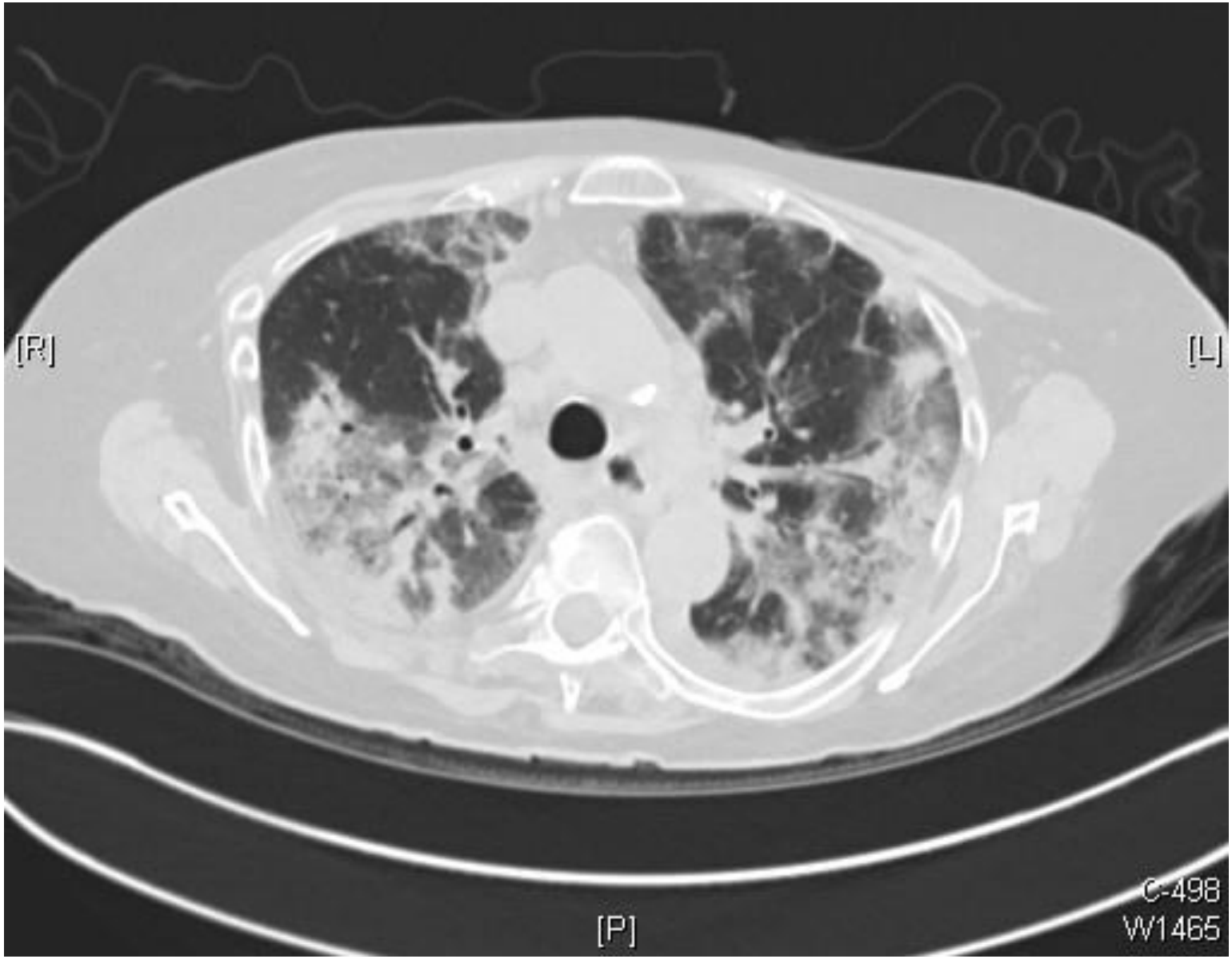
CXR 8d later

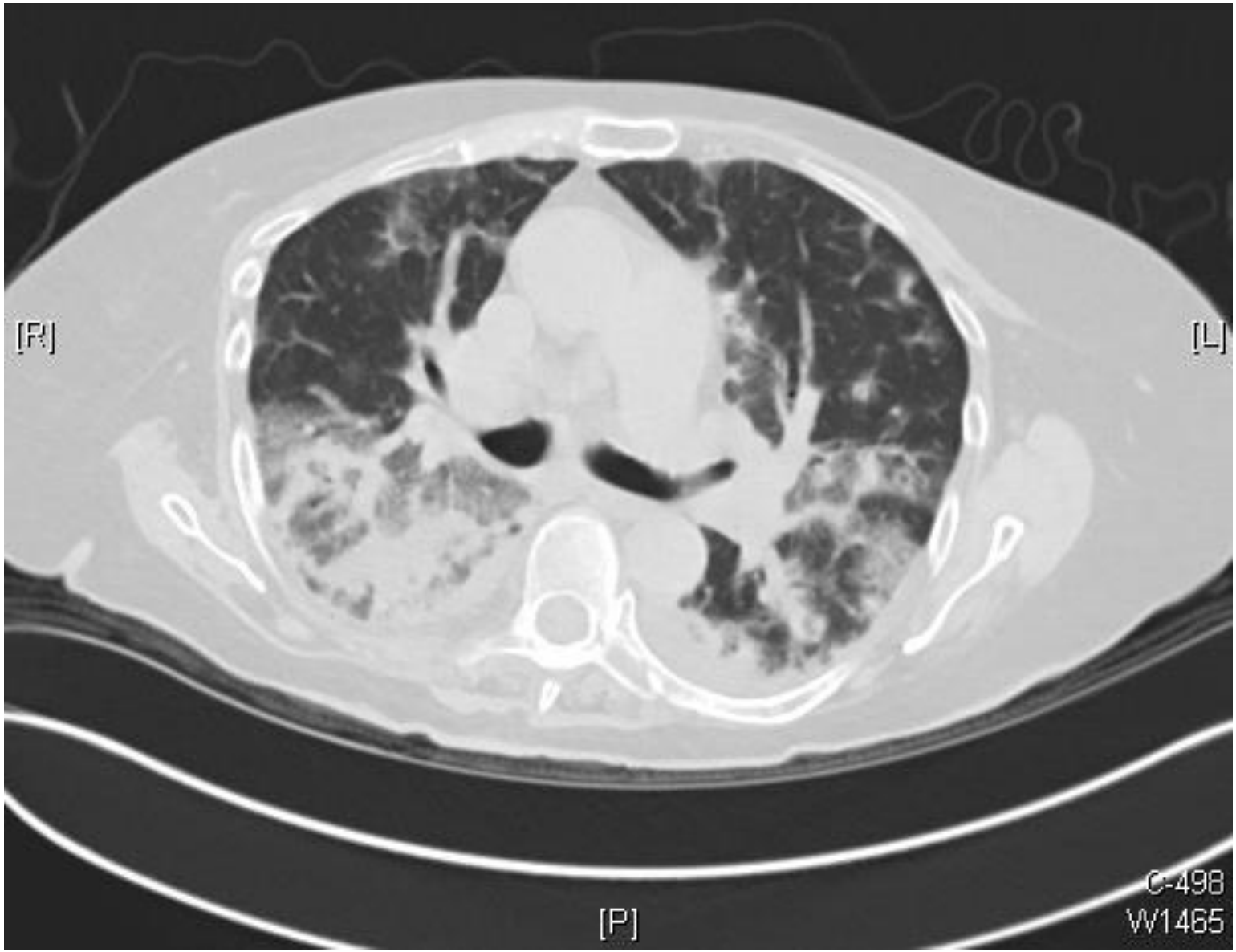


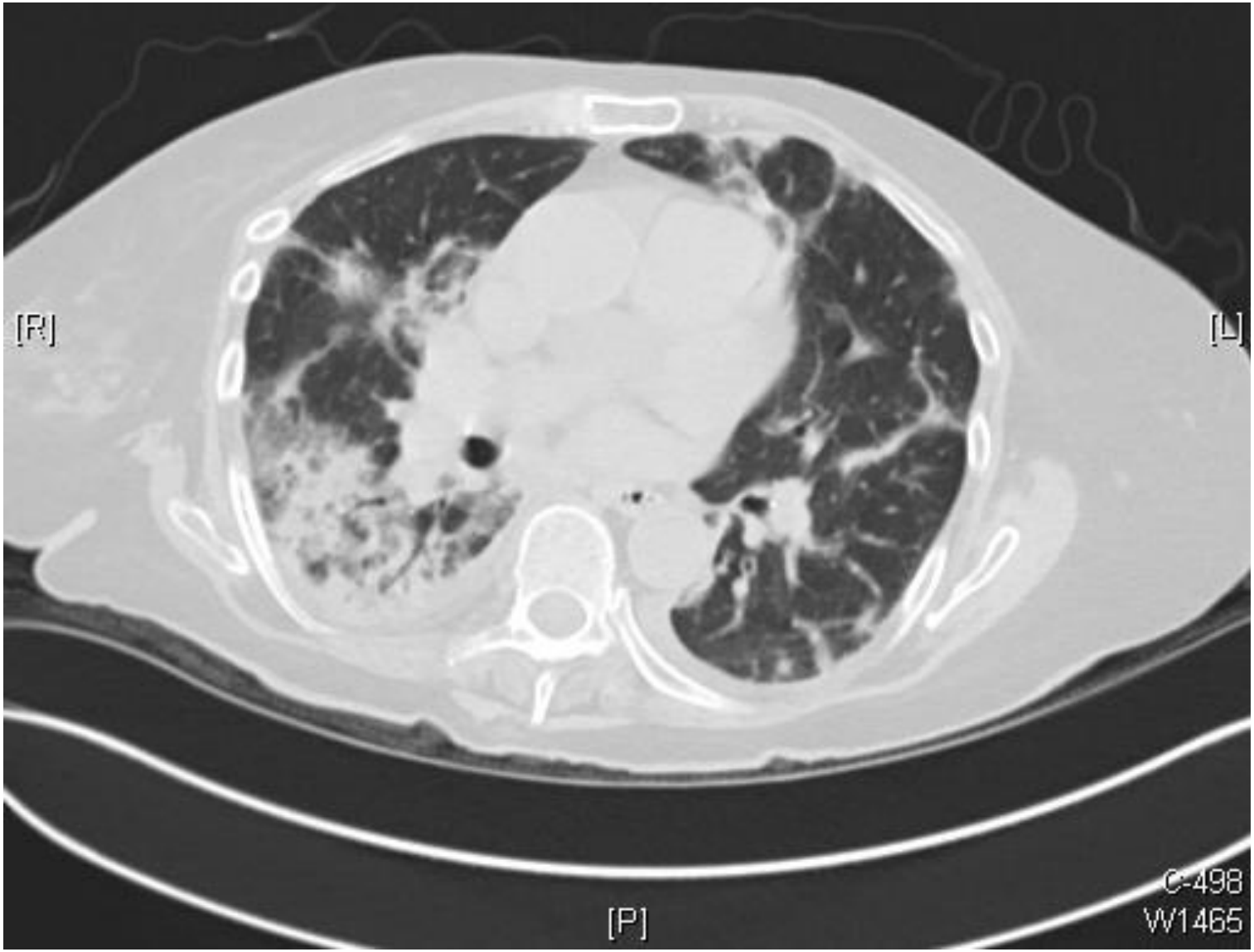
CT

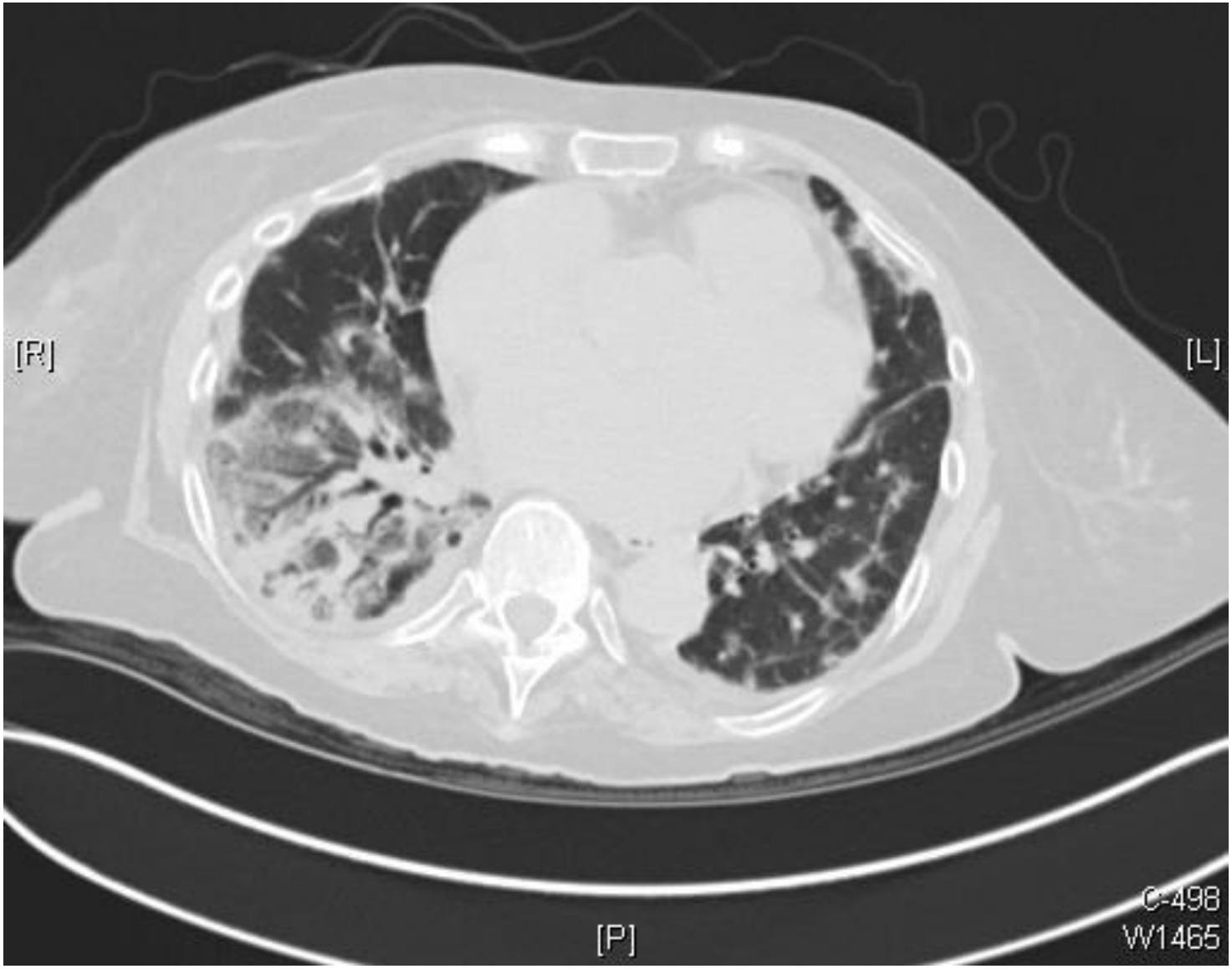


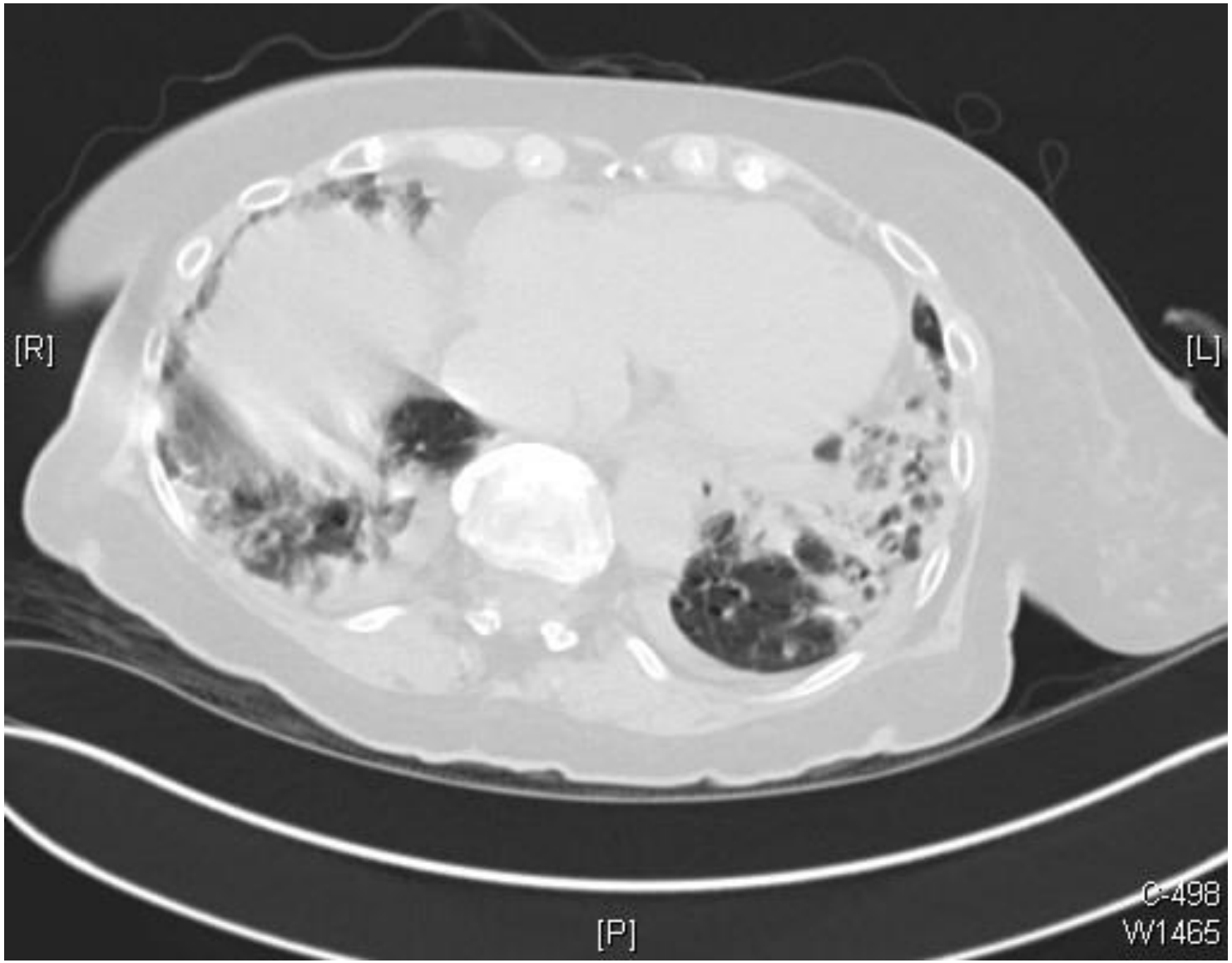

[R]
[L]
[P]
C-498
W1465


[R]
[L]
[P]
C-498
W1465


[R]
[L]
[P]
C-498
W1465


[R]
[L]
[P]
C-498
W1465


[R]
[L]
[P]
C-498
W1465


[R]
[L]
[P]
C-498
W1465

Case, continued:

- She is admitted and given CAP coverage.
- 3d later, her O2 requirements increase to 5L
- WBC 9 to 15K, 95% neutrophils, 5% lymphocytes

Reasons for Failure to Improve

- Resistant microorganism
  - Uncovered pathogen
  - Inappropriate by sensitivity
- Parapneumonic effusion/empyema
- Nosocomial superinfection
  - Nosocomial pneumonia
  - Extrapulmonary
- Noninfectious
  - Complication of pneumonia (e.g., BOOP)
  - Misdiagnosis: PE, CHF, vasculitis
  - Drug fever

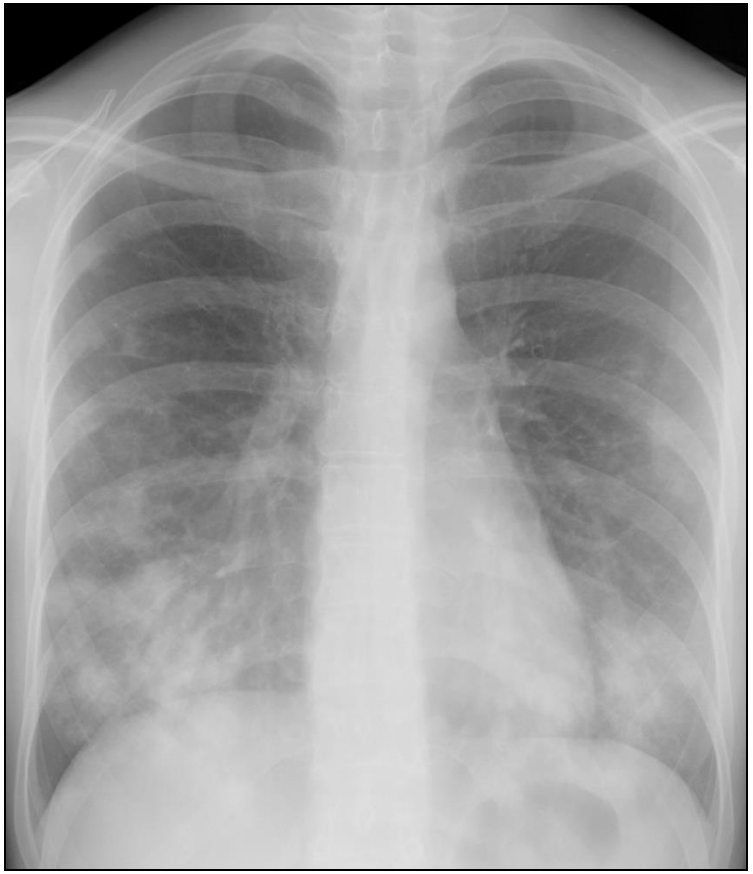
IDSA Guidelines, 2007

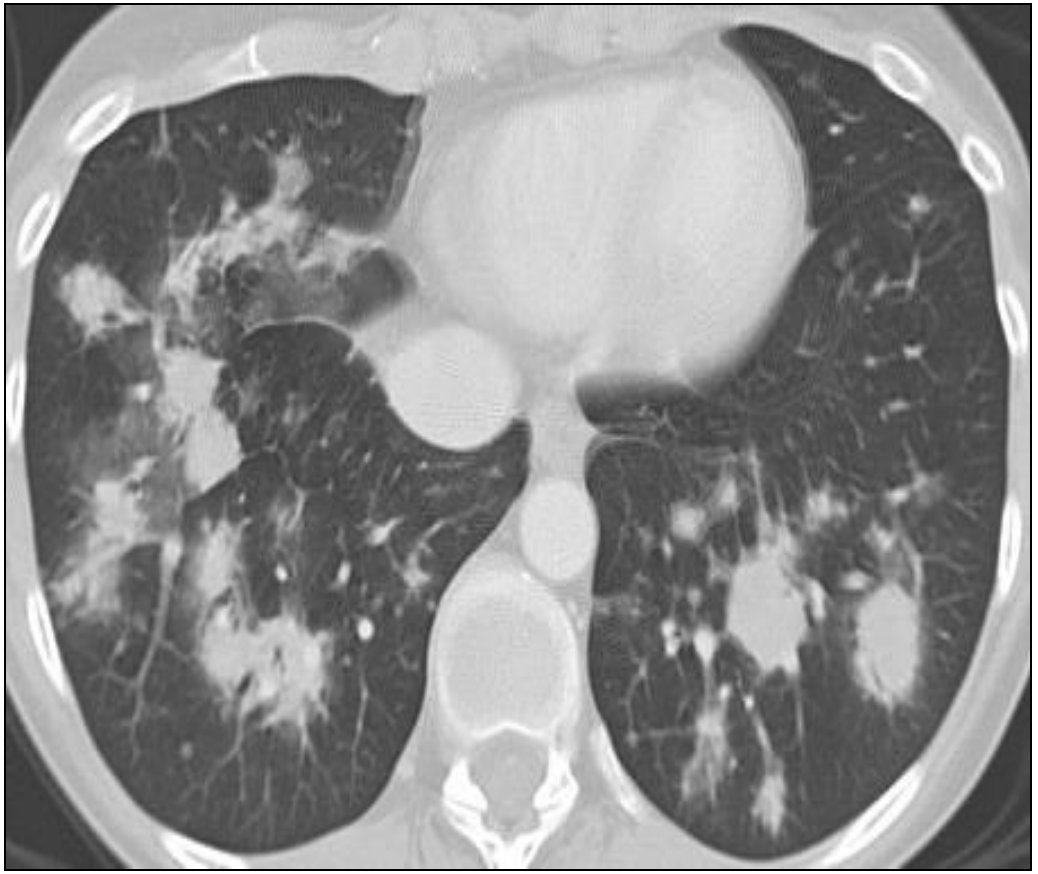
Table 1. Differential Diagnosis of Community-Acquired Pneumonia.

Abnormal chest radiograph
Congestive heart failure with associated viral syndrome to explain infectious symptoms
Aspiration pneumonitis
Pulmonary infarction
Acute exacerbation of pulmonary fibrosis
Acute exacerbation of bronchiectasis
Acute eosinophilic pneumonia
Hypersensitivity pneumonitis
Pulmonary vasculitis
Cocaine-induced lung injury ("crack lung")
Normal chest radiograph
Acute exacerbation of chronic obstructive pulmonary disease
Influenza
Acute bronchitis
Pertussis
Asthma with associated viral syndrome to explain infectious symptoms

N Engl J Med 2014; 370;6

Mimics of Pneumonia: Relapsed Lymphoma





Case, continued:

- Antibiotic coverage is empirically broadened.

Case, continued:

- 3d later, she's still not improved
  - Transthoracic Echo normal
  - No response to diuresis
  - Speech/swallow evaluation performed and negative
- What next?

9d after admission

- Bronchoscopy
  - 685 RBC, 295 WBC (32% Neutrophils, 13% Lymphs, 8% Monos, 39% eosinophils)

Acute Eosinophilic pneumonia

- Known causes: e.g., meds, parasites
- DDx: “PIE”, e.g., Churg Strauss, CEP, ABPA, etc
- Idiopathic:
  - Similar presentation as CAP
  - Classically no circulating eosinophils detected, but eos seen in BAL
  - Can respond dramatically to steroids
  - One approach is to treat for 1 month after symptoms disappear and CXR normal (i.e., on the order of 4-6 weeks); inhaled steroids may be beneficial in relapse

Before: Steroids for Hospitalized CAP?

Annals of Internal Medicine REVIEW

Corticosteroid Therapy for Patients Hospitalized With Community-Acquired Pneumonia

A Systematic Review and Meta-analysis

- Metanalysis/review 13 trials (n=2005 subjects)
- Reductions in mechanical ventilation, ARDS
- Reduction in time to stability and discharge*
- Possible reduced mortality (severe PNA)
  - May be different for subgroups (e.g., S. pneumo, flu)
- Variable agents, routes, doses, courses
- Ongoing clinical trials—use biomarkers to select subjects for treatment?

Oct 2015 – Cochrane 2017

The NEW ENGLAND JOURNAL of MEDICINE

NOW:

ORIGINAL ARTICLE

Hydrocortisone in Severe Community-Acquired Pneumonia

- 795 patients, randomized phase 3 RCT
- Hydrocortisone vs. Placebo 200 mg/day for 4 or 7d based on clinical improvement (then taper, total 8 or 14 days)
- HC: Improved 28d mortality and intermediate endpoints – more insulin in the HC group
- ? Benefits in pt subgroups without a pathogen and elevated CRP (>15 mg/dL)

N Engl J Med. 2023; Mar 21. doi: 10.1056/NEJMoa2215145.

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 12: For inpatients with CAP should steroids be added?

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Question 12: For inpatients with CAP should steroids be added?

2019: Not routinely for severe or nonsevere CAP. Mixed trial results. (2022 trial by Meduri et al in Int Care Med suggested no mortality benefit in severe CAP).

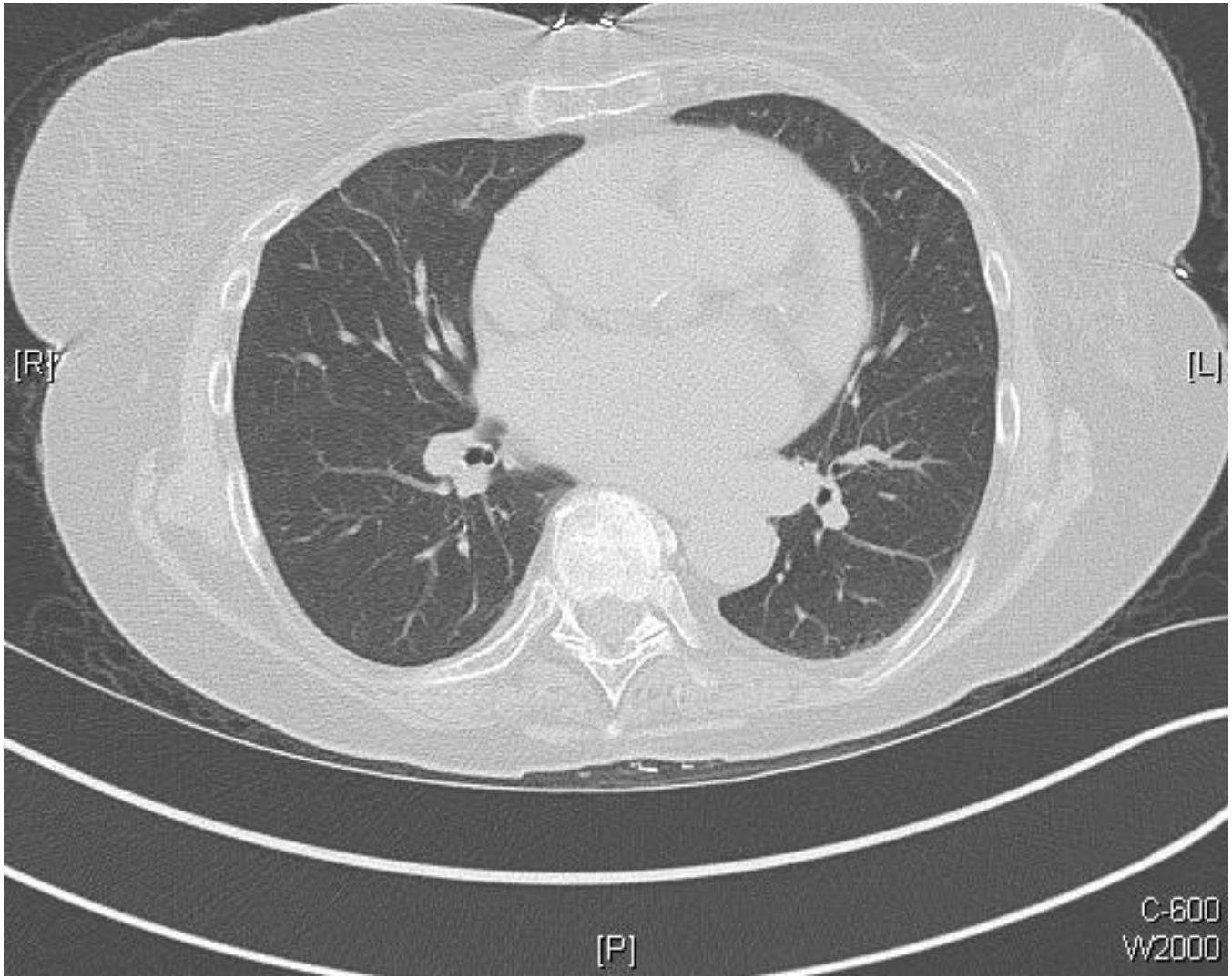
2023: NEJM paper suggests leaning toward 'yes' for severe community-acquired pneumonia

2024: LRM paper - Prespecified subgroup of pts in APPROCCHSS (septic shock) with CAP and septic shock had lower mortality with hydrocortisone+fludrocortisone vs. placebo

Case, Continued

- She is prescribed steroids and in 3-4 days has improved to point of discharge. She is also given PCP/PJP prophylaxis.
- She is tapered over the next 4 months and does well overall.

5 months later



Pneumonia prevention

1. Pneumococcal vaccination
2. Influenza vaccination
3. Smoking cessation

[Other vaccinations as indicated...]

Today's Take Home Points

- CAP is primarily a clinical diagnosis.
- All patients with pneumonia should have a CXR.
- Can use evidence-based triage algorithms, but don't substitute for clinical judgment.
- Consider epidemiology, co-morbidity and recent exposure when choosing antibiotics; give appropriate antibiotics EARLY. Stay flexible with your diagnosis if no improvement. Consider hydrocortisone for severe CAP.
- Don't miss the chance to use hospitalization as an opportunity to vaccinate your patients.
- Leaning away from HCAP as an entity and more toward tailoring coverage based on local epidemiology, then deescalating after negative culture data.

Question #1

- A positive sputum culture is required to make a diagnosis of community-acquired pneumonia:
  - True
  - False

Question #1

- A positive sputum culture is required to make a diagnosis of community-acquired pneumonia:
  - True
  - False

Question #2

- You're called to the emergency department to admit a 75 year-old nursing home resident who is on steroids for COPD and who was hospitalized 2 months ago due to altered mental status and had a MRSA infection. She now presents with fevers, purulent sputum and a right middle lobe infiltrate. Your empiric antibiotic regimen of choice is:
  - 1. Nothing now—wait for cultures
  - 2. Oral levofloxacin
  - 3. i.v. levofloxacin
  - 4. Vancomycin, ceftaz, and levofloxacin
  - 5. Vancomycin

Question #2

- You're called to the emergency department to admit a 75 year-old nursing home resident who is on steroids for COPD and who was hospitalized 2 months ago due to altered mental status and had a MRSA infection. She now presents with fevers, purulent sputum and a right middle lobe infiltrate. Your empiric antibiotic regimen of choice is:
  - 1. Nothing now—wait for cultures
  - 2. Oral levofloxacin
  - 3. i.v. levofloxacin
  - 4. Vancomycin, ceftaz, and levofloxacin
  - 5. Vancomycin

Question #3

- A 25 year-old man with well-controlled diabetes, who has never been hospitalized before, presents with cough, dyspnea, fevers, pleuritic chest pain, and a right lower lobe infiltrate. He is admitted to your service for treatment of pneumonia. Your initial antibiotic regimen of choice is:
  - 1. Nothing now—wait for cultures
  - 2. Augmentin
  - 3. Doxycycline
  - 4. Vancomycin + Gentamicin
  - 5. Ceftriaxone + Azithromycin

Question #3

- A 25 year-old man with well-controlled diabetes, who has never been hospitalized before, presents with cough, dyspnea, fevers, pleuritic chest pain, and a right lower lobe infiltrate. He is admitted to your service for treatment of pneumonia. Your initial antibiotic regimen of choice is:
  - 1. Nothing now—wait for cultures
  - 2. Augmentin
  - 3. Doxycycline
  - 4. Vancomycin + Gentamicin
  - 5. Ceftriaxone + Azithromycin

Question #4

- A 75 year-old man with emphysema is admitted for a COPD flare. He improves with steroids, bronchodilators, and antibiotics. As you're getting ready to discharge him, you discuss with him the following vaccinations:
  - 1. Pneumovax
  - 2. Influenza (if available)
  - 3. Neither
  - 4. Both

Question #4

- A 75 year-old man with emphysema is admitted for a COPD flare. He improves with steroids, bronchodilators, and antibiotics. As you're getting ready to discharge him, you discuss with him the following vaccinations:
  - 1. Pneumovax
  - 2. Influenza (if available)
  - 3. Neither
  - 4. Both

Question #5

- A 75 year-old smoker with emphysema is admitted for a COPD flare and a left lower lobe pneumonia. He improves with steroids, bronchodilators, and antibiotics. You're setting up a follow-up appointment for him with you in clinic and plan:
  - 1. A follow-up CXR in 3 months
  - 2. A follow-up CT scan of the chest next week
  - 3. A follow-up sputum culture
  - 4. A follow-up visit for spirometry only
  - 5. No follow-up visit necessary—have him call you if he develops respiratory symptoms

Question #5

- A 75 year-old smoker with emphysema is admitted for a COPD flare and a left lower lobe pneumonia. He improves with steroids, bronchodilators, and antibiotics. You're setting up a follow-up appointment for him with you in clinic and plan:
  - 1. A follow-up CXR in 3 months*
  - 2. A follow-up CT scan of the chest next week
  - 3. A follow-up sputum culture
  - 4. A follow-up visit for spirometry only
  - 5. No follow-up visit necessary—have him call you if he develops respiratory symptoms

*although recent guidelines suggest not necessary if would be captured by malignancy screening anyhow

References

- Overview: Wunderink et al. BMJ 2017
- CAP/HAP Guidelines and Treatment
  - Wunderink *et al*. NEJM 2014;370:543
  - Mandell *et al*. CID 2007;44:S27
  - Waterer *et al*. AJRCCM 2011;183:157
  - Meehan *et al*. JAMA 1997;278:2080
  - Feldman and Richards. F1000Res 2018 23;7.
  - Kalil *et al*. CID 2016;63:575
  - Metlay *et al*. AJRCCM 2019; 200:e45-67.
  - Deshpande *et al*. CID 2021;72:1314.
  - Kato *et al*. J Glob Antimicrob Resist 2021;24:98.
  - Dequin *et al*. NEJM 2023; Mar 21.