

PNEUMONIA: Community and Hospital Acquired, Including a Case Study

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**CONTINUING MEDICAL EDUCATION
DEPARTMENT OF MEDICINE**



**BRIGHAM AND
WOMEN'S HOSPITAL**

| **The Lung Center** |



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Disclosures

- Advisory Boards for Merck, Genentech
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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 <i>Pseudomonas aeruginosa</i>
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 <i>P. aeruginosa</i>
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 <i>P. aeruginosa</i> 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)

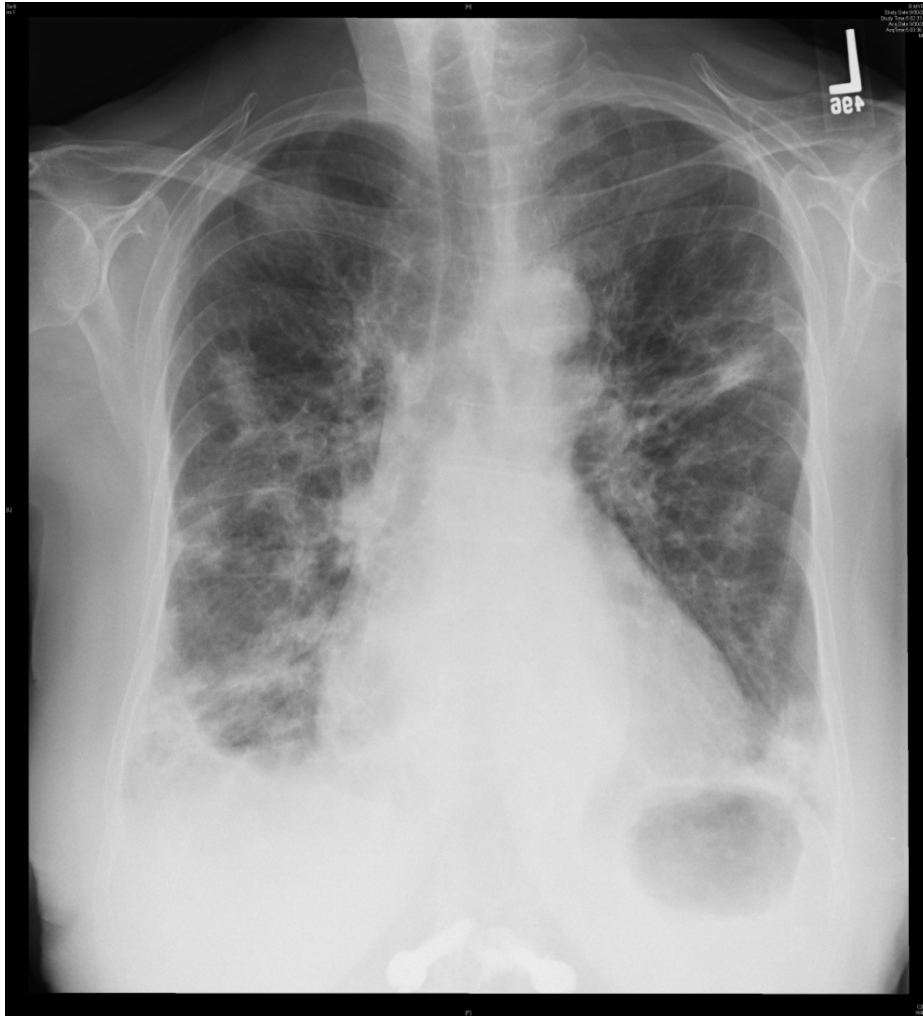
The Case

- 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.

Niedeman, 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%

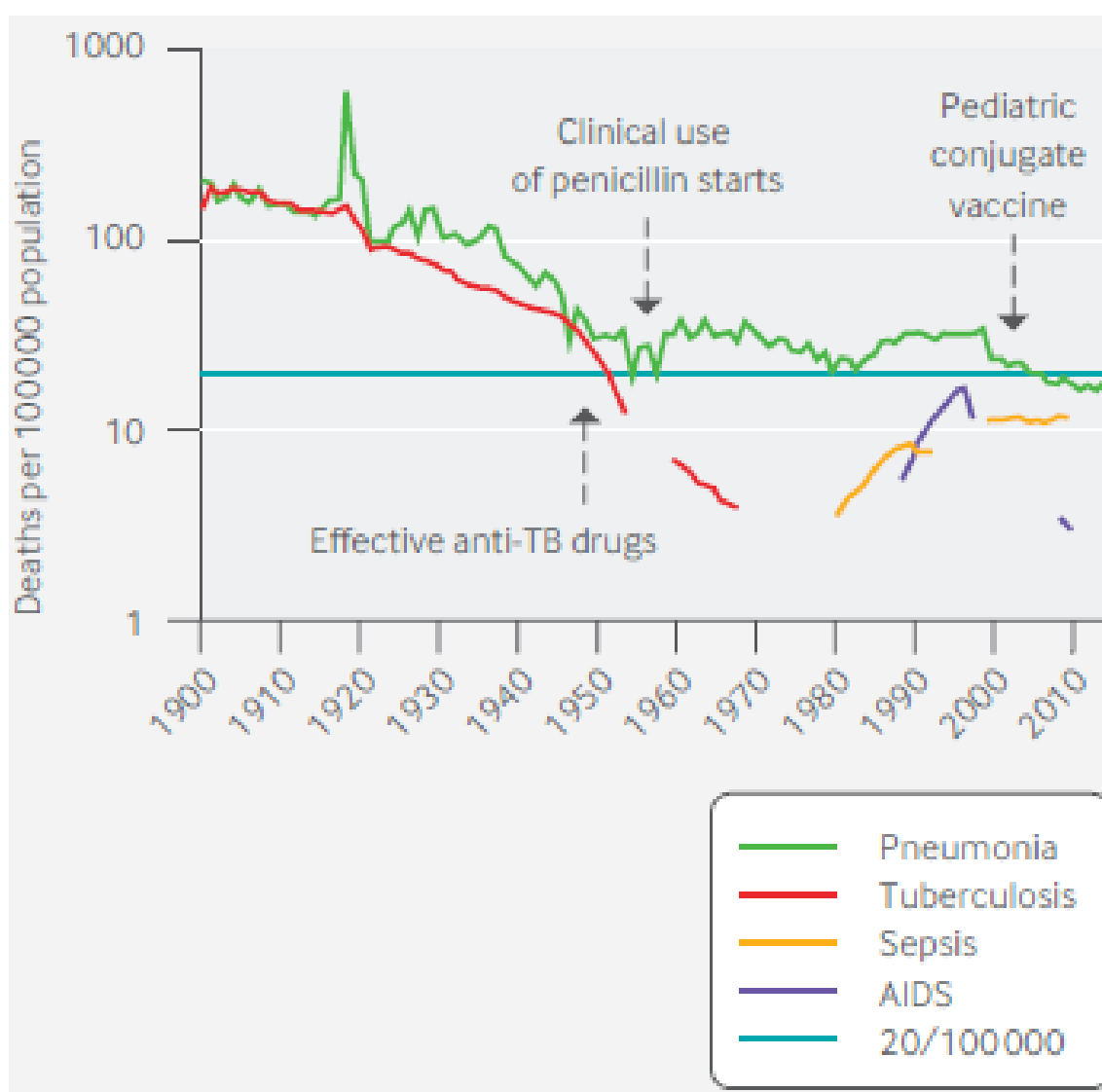


Fig 1 | Temporal trends in US mortality from pneumonia and influenza compared with other important infections since 1900 (source: Centers for Disease Control and Prevention).

TB=tuberculosis

MECHANISM OF INFECTION

- **Air borne** – via the tracheobronchial tree (infected bronchoscope, aspiration or inhalation of microorganisms) 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
<i>S. pneumonia</i>	4	20.3	22.5
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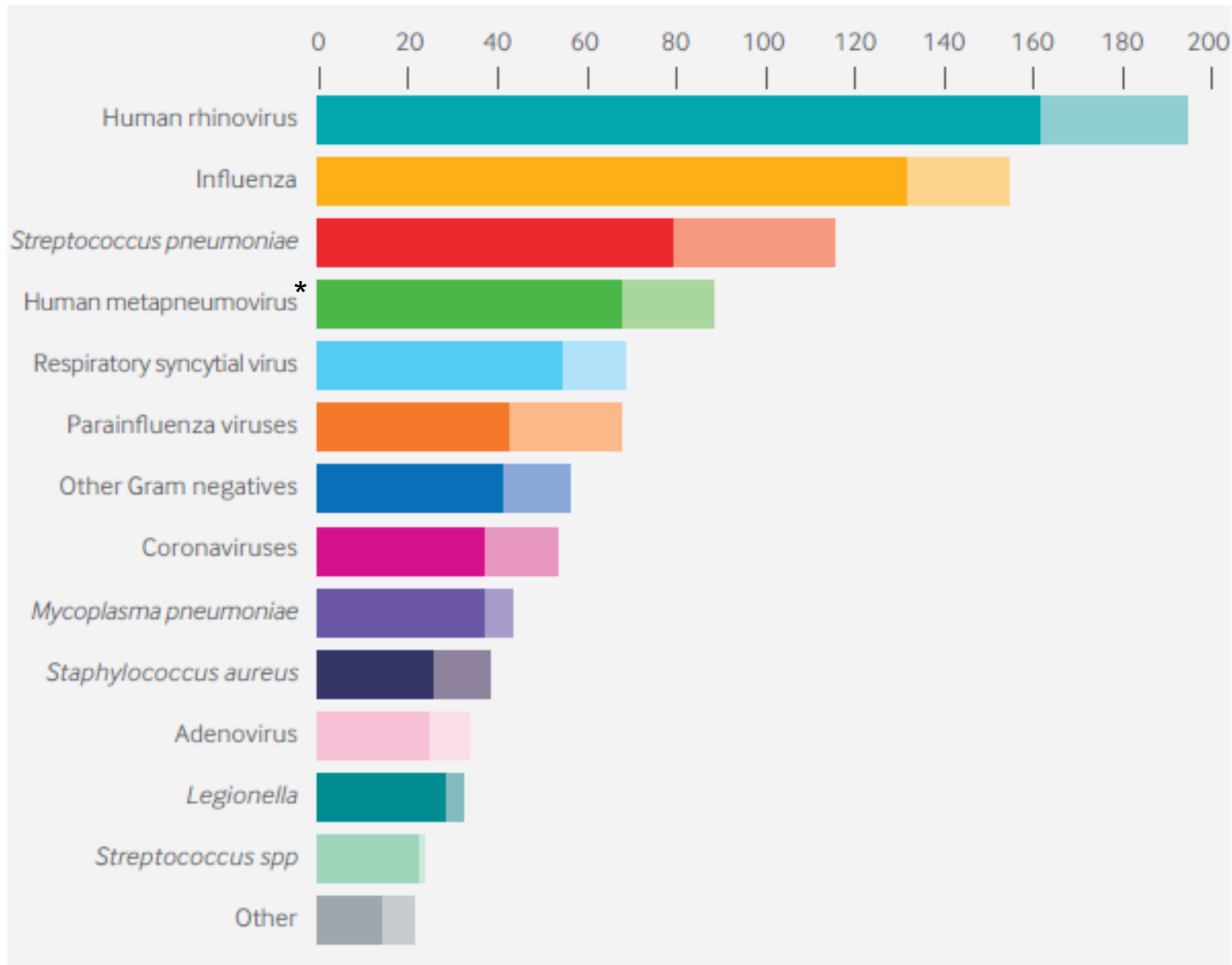


Fig 3| Pathogens detected in patients with radiographic community acquired pneumonia from the Centers for Disease Control EPIC study. Lighter bars indicate co-detections of more than one pathogen. From Jain et al¹⁹ NEJM 2015

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

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...

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

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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

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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?

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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

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

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

No 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

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

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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	<i>Legionella</i> 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 <i>Legionella</i> 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.

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

Risk Stratification in CAP

- Many prediction models available
- Large retrospective and prospective cohorts demonstrate that medical comorbidities, 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.)

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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?

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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 misriage.

Criteria for Severe CAP

Minor criteria^a

Respiratory rate^b ≥ 30 breaths/min

PaO₂/FiO₂ ratio^b ≤ 250

Multilobar infiltrates

Confusion/disorientation

Uremia (BUN level, ≥ 20 mg/dL)

Leukopenia^c (WBC count, < 4000 cells/mm³)

Thrombocytopenia (platelet count, $< 100,000$ cells/mm³)

Hypothermia (core temperature, $< 36^\circ\text{C}$)

Hypotension requiring aggressive fluid resuscitation

Major criteria

Invasive mechanical ventilation

Septic shock with the need for vasopressors

NOTE. BUN, blood urea nitrogen; PaO₂/FiO₂, 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 PaO₂/FiO₂ ratio < 250 .

^c As a result of infection alone.

Etiology of CAP (%)

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Polymicrobial	1.5	8.6	5.4

Beta-lactam activity

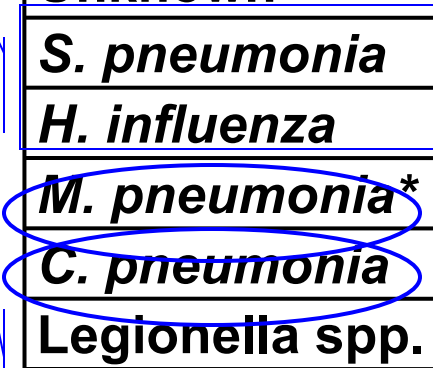
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Macrolide activity

Etiology of CAP (%)

So-so



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<i>H. influenzae</i>	4	6	5.3
<i>M. pneumoniae</i>*	15.3	3.9	1.9
<i>C. pneumoniae</i>	4.5		
Legionella spp.	0.9	3.4	5.9
<i>S. aureus</i>		1.8	2.5
GNR		3.2	10
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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)
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Fluoroquinolone activity

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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*.

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

	Standard Regimen
No comorbidities or risk factors for MRSA or <i>Pseudomonas aeruginosa</i> *	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.

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 <i>Pseudomonas aeruginosa</i>	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for <i>P. aeruginosa</i>
Nonsevere inpatient pneumonia*	β-Lactam + macrolide [†] or respiratory fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> 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 <i>P. aeruginosa</i> only if culture results are positive
Severe inpatient pneumonia*	β-Lactam + macrolide [†] or β-lactam + fluoroquinolone [‡]	Add MRSA coverage [§] and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for <i>P. aeruginosa</i> 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 <i>P. aeruginosa</i> 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

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

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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.

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

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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.

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

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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?

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

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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.

AMERICAN THORACIC SOCIETY DOCUMENTS

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

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

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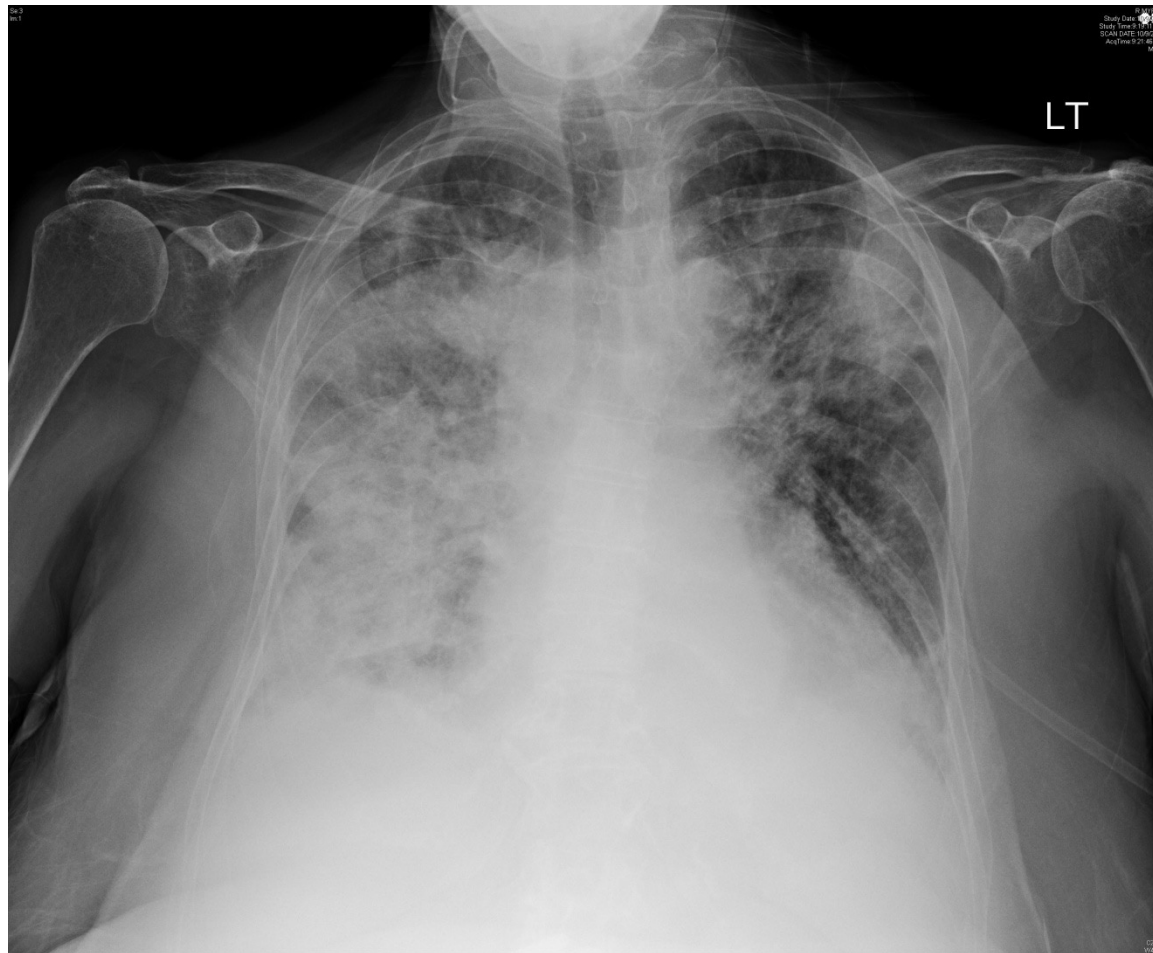
Question 5: In adults with CAP should serum procalcitonin testing be used to withhold antibiotics?

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.

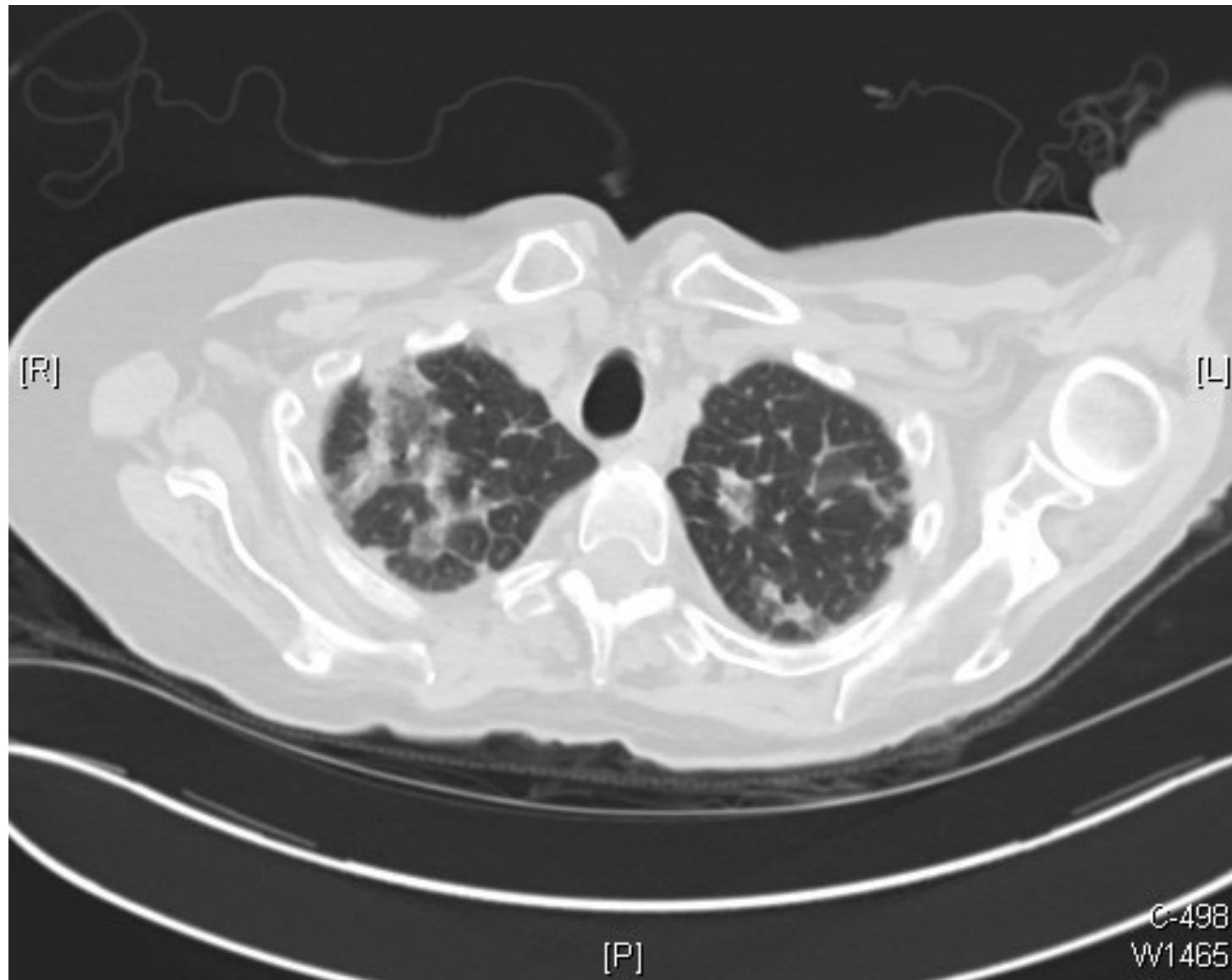
Case, continued:

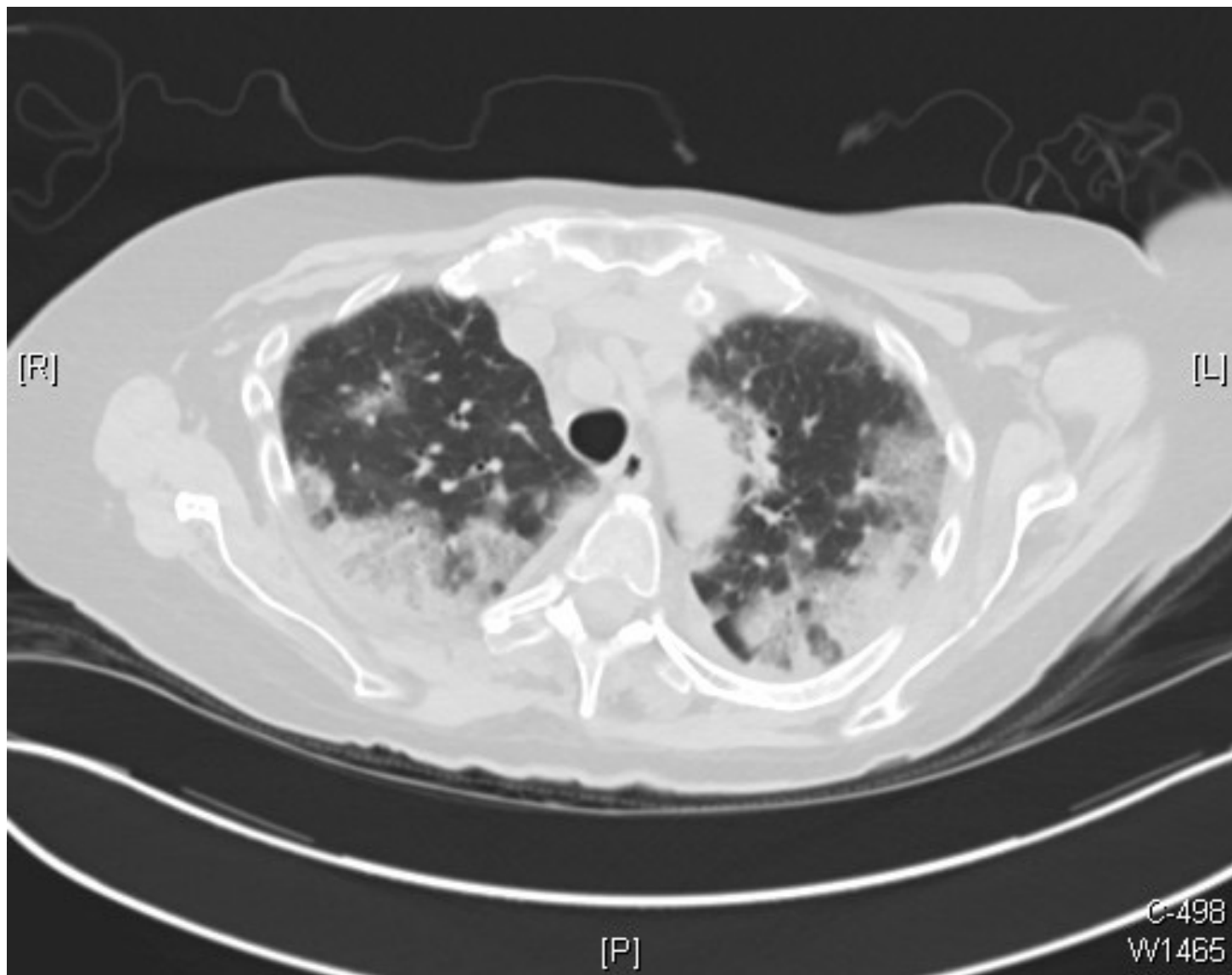
- She is given 5d of azithromycin and doxycycline
- 8 days later, she is seen in pulmonary clinic
 - T101
 - Room Air sats 80s, dyspneic

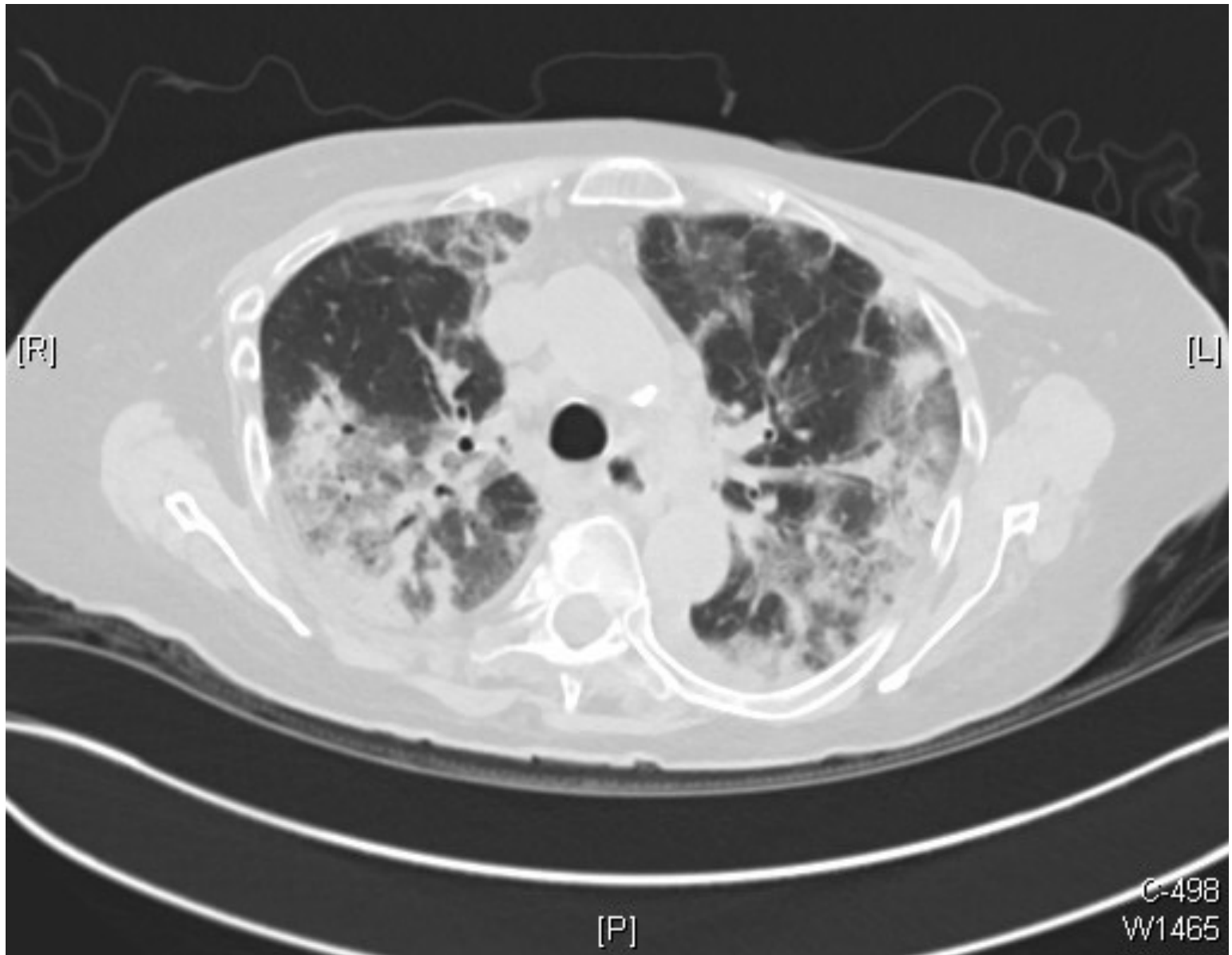
CXR 8d later



CT





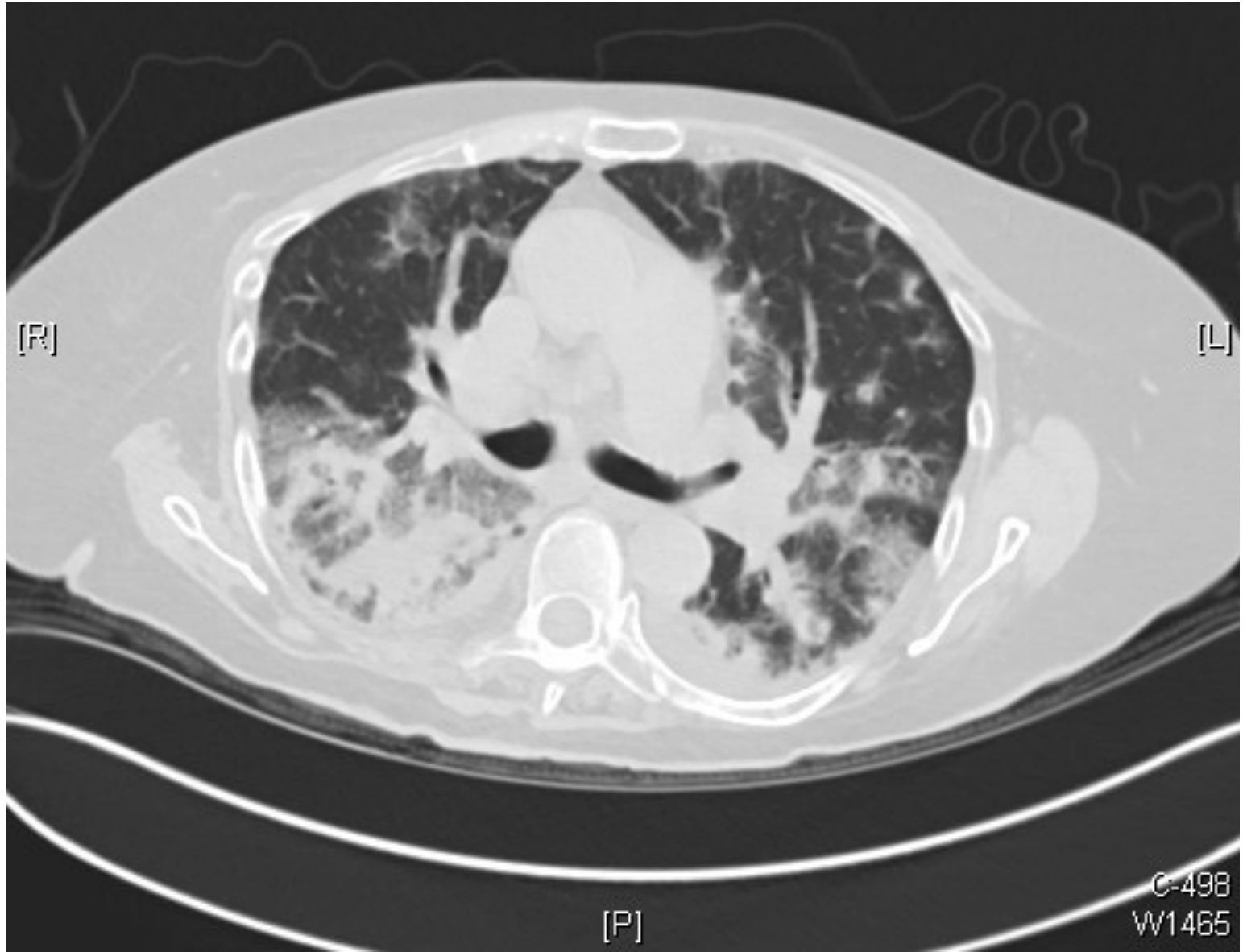


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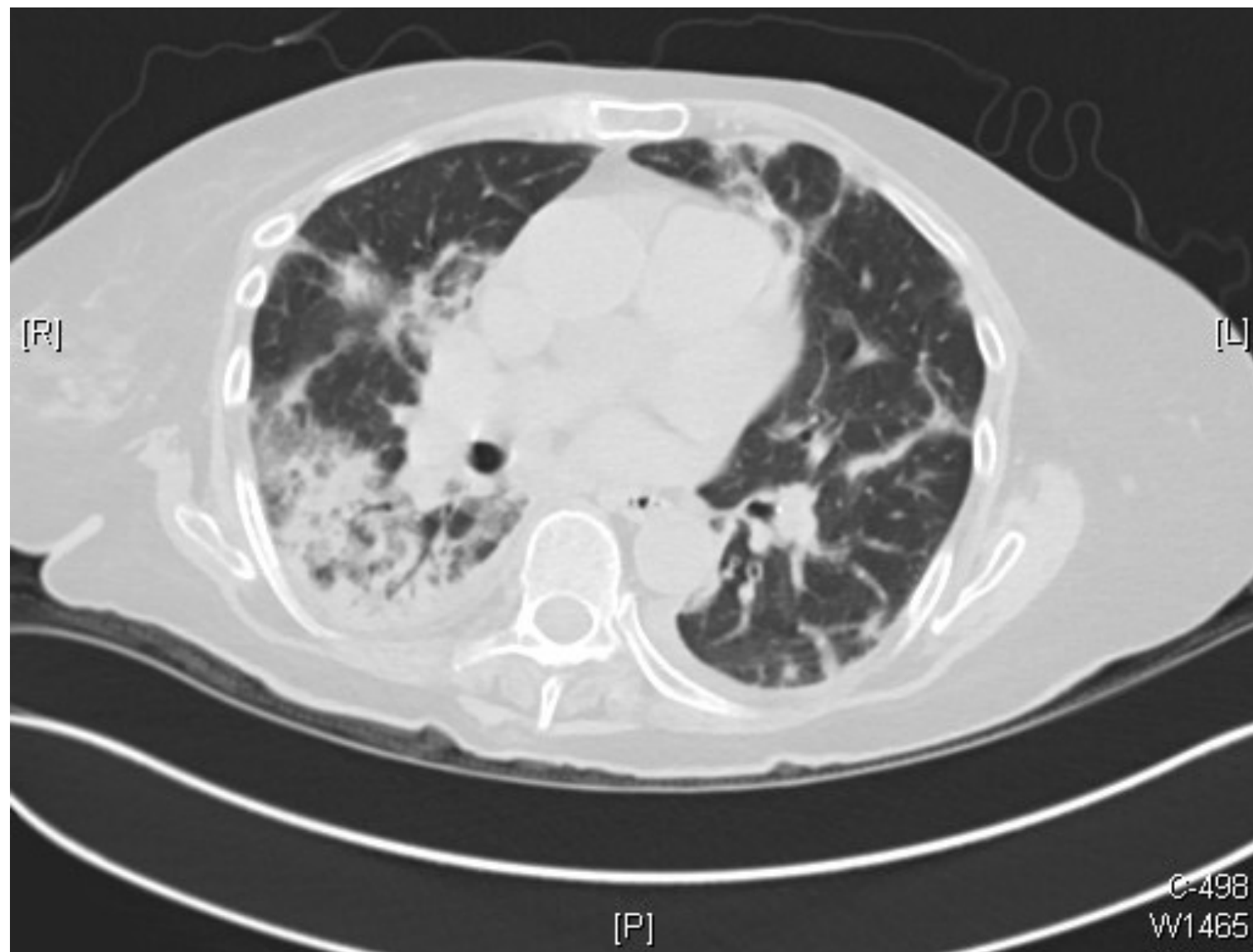


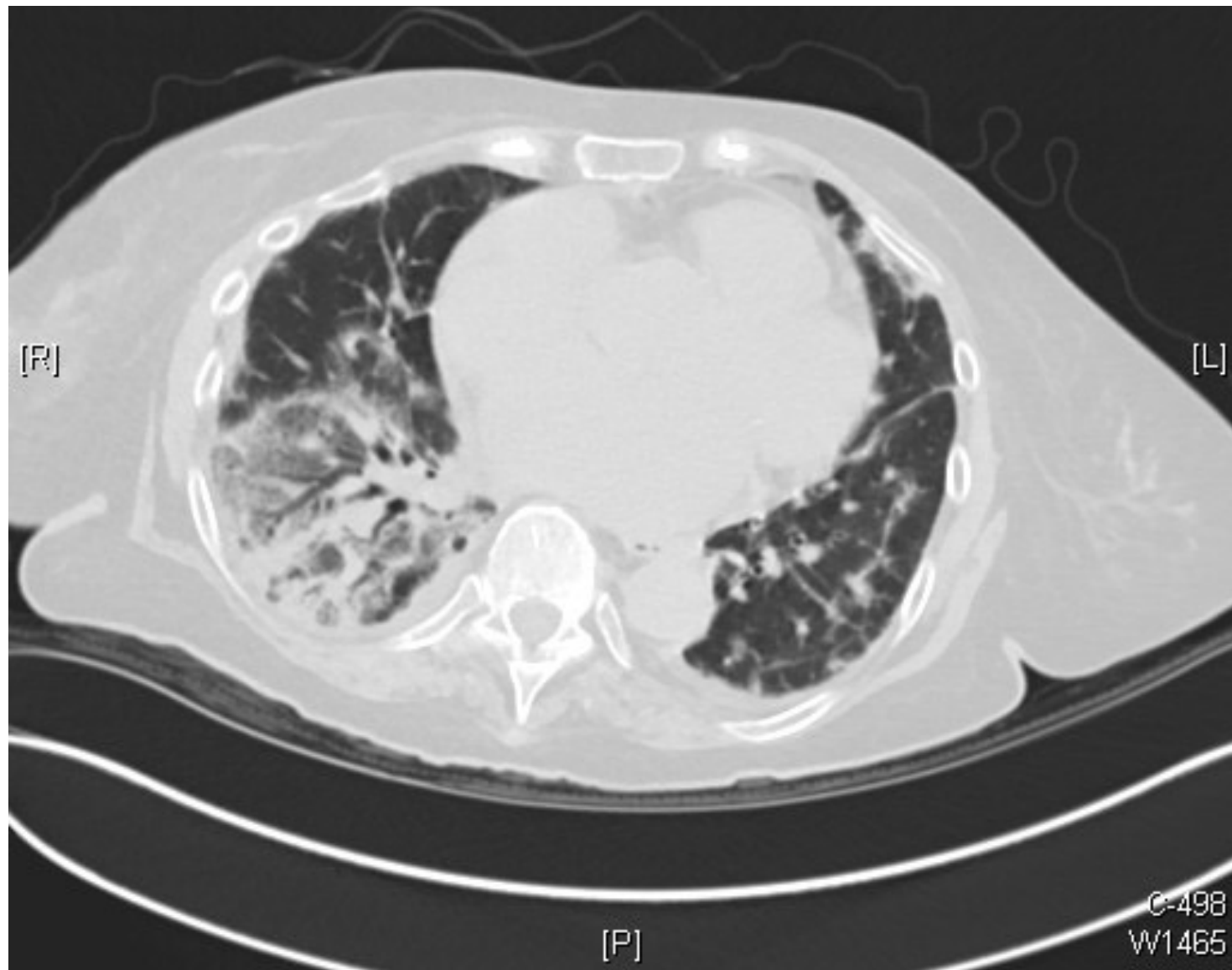
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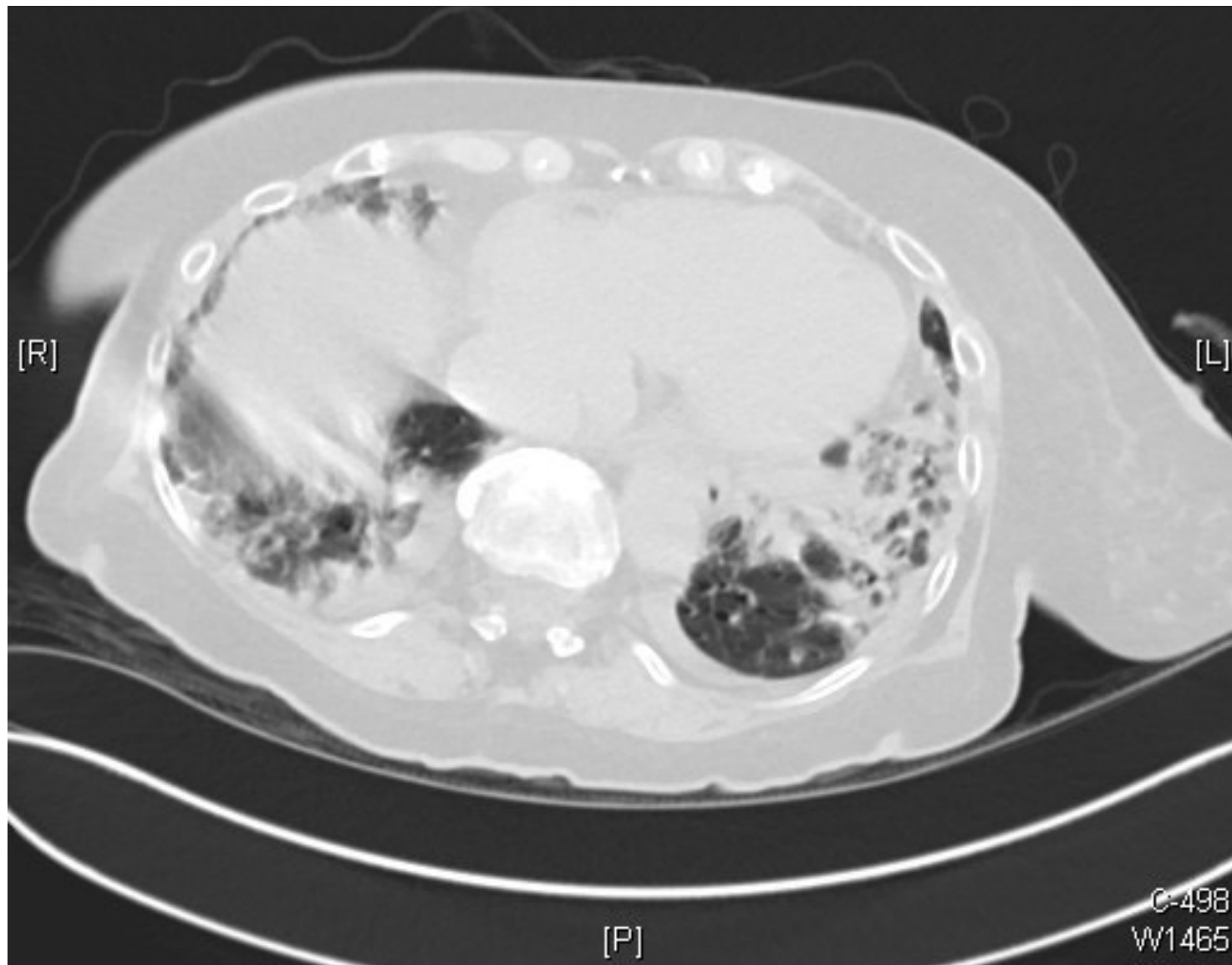
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Case, continued:

- 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

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

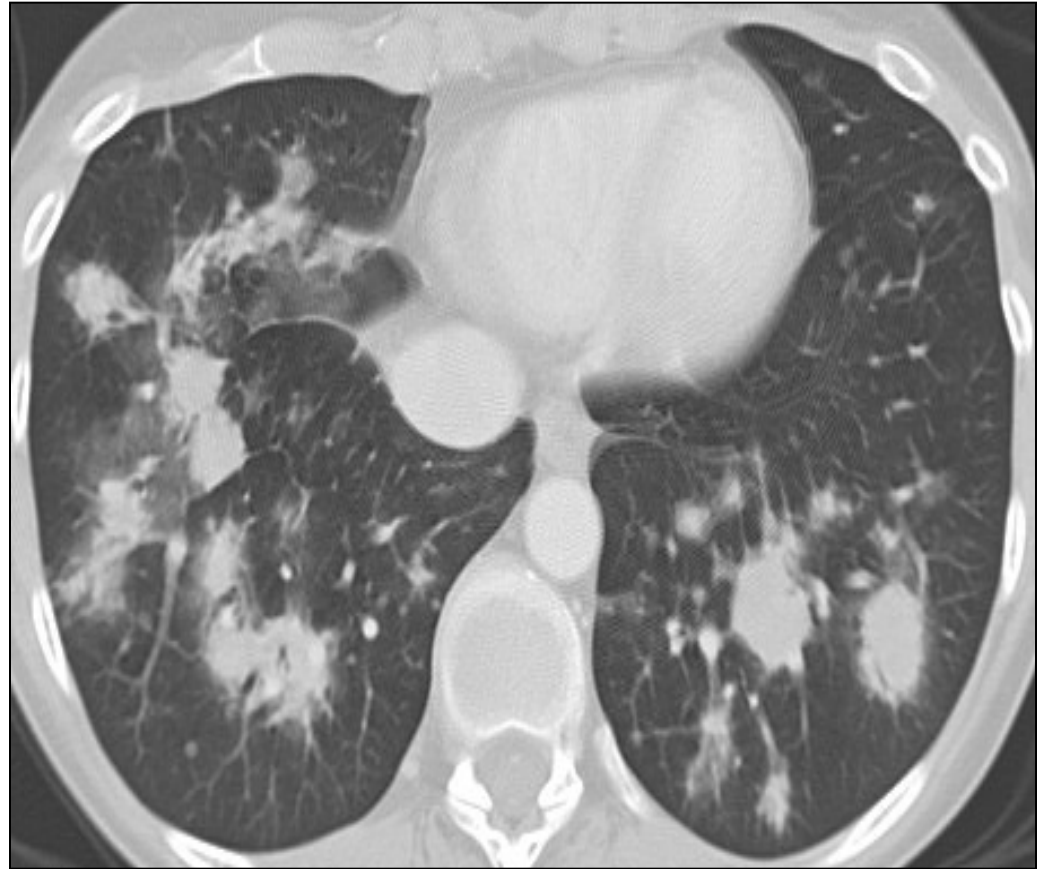
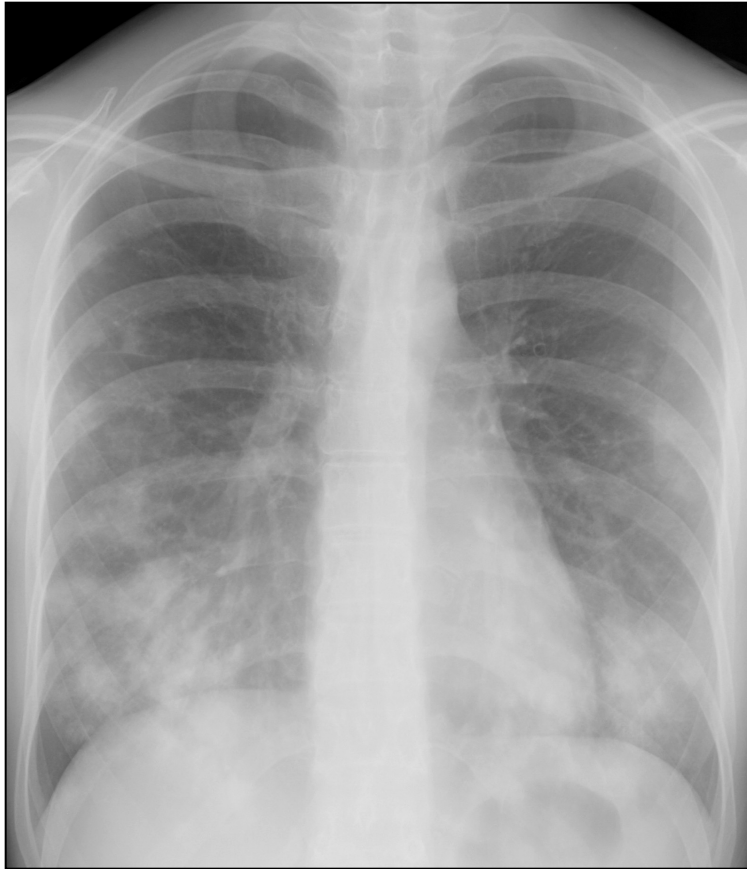
Influenza

Acute bronchitis

Pertussis

Asthma with associated viral syndrome to explain infectious symptoms

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

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

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

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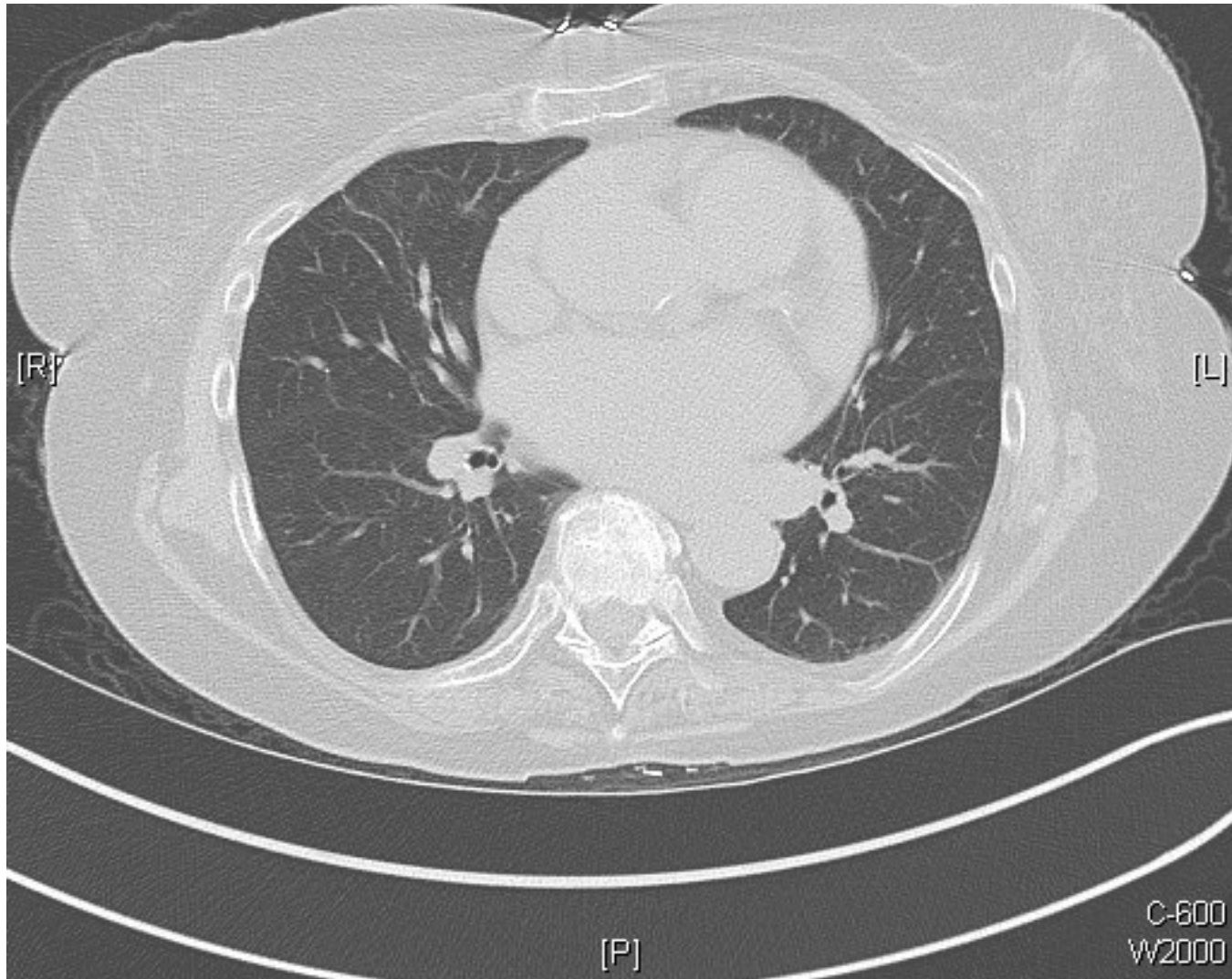
Question 12: For inpatients with CAP should steroids
be added?

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).

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.
- 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.

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 <i>Pseudomonas aeruginosa</i>
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 <i>P. aeruginosa</i>
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 <i>P. aeruginosa</i> 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*.

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

Disclosures

- Advisory Board to Merck, Genentech
- Thanks to Joel Katz, M.D., Chanu Rhee, M.D. (Infectious Diseases, BWH) and Ritu Gill, M.D. (Chest Radiology, BWH) for sharing slides.

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
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 - Deshpande *et al.* CID 2021;72:1314.
 - Kato *et al.* J Glob Antimicrob Resist 2021;24:98.

CAP--Epidemiology

- 3 fold variances in admission rates across the USA, results in large cost differential
 - Average Outpatient cost: \$264
 - Average Inpatient cost: \$7500
 - Mortality rate 13.4 per 100,000

Health care providers (MD's, RN's, *etc*) tend to overestimate mortality

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

Treatment of Community-Acquired Pneumonia in Immunocompromised Adults

A Consensus Statement Regarding Initial Strategies

Ramirez JA, et al. Chest, Aug 2020

ORIGINAL ARTICLE

Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

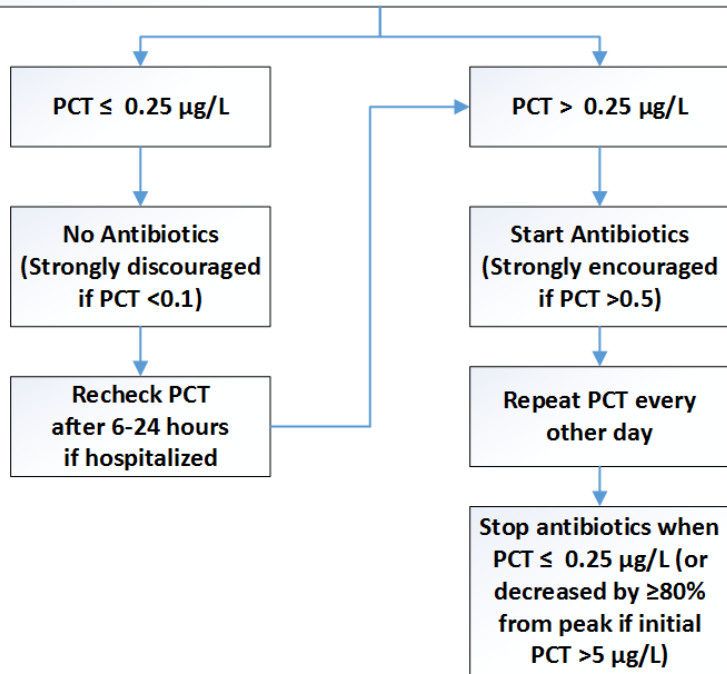
D.T. Huang, D.M. Yealy, M.R. Filbin, A.M. Brown, C.-C.H. Chang, Y. Doi,
M.W. Donnino, J. Fine, M.J. Fine, M.A. Fischer, J.M. Holst, P.C. Hou, J.A. Kellum,
F. Khan, M.C. Kurz, S. Lotfipour, F. LoVecchio, O.M. Peck-Palmer, F. Pike,
H. Prunty, R.L. Sherwin, L. Southerland, T. Terndrup, L.A. Weissfeld, J. Yabes,
and D.C. Angus, for the ProACT Investigators*

- 2017: FDA approved PCT to help guide initiation or discontinuation of abx in the ED or hospital for LTRI, based on data that PCT reduced abx use without harm
- Randomized to PCT prescribing guideline vs. usual care (1656 patients in the ED)
- NO DIFFERENCE in antibiotic use

Suggested Algorithm for PCT Use at BWH

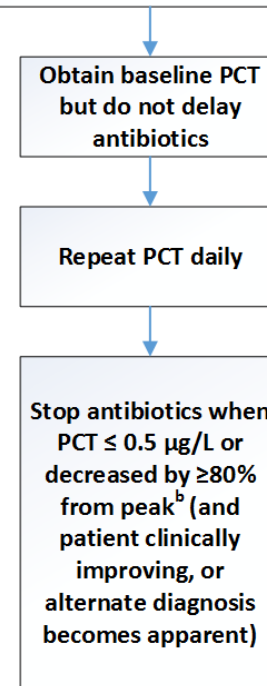
SUSPECTED RESPIRATORY INFECTION IN STABLE PATIENT

- Not critically ill → refer to “Suspected Sepsis” algorithm
- Not high-risk (e.g., CAP PSI \geq IV / CURB 65 \geq 2, COPD GOLD >III) → do not withhold antibiotics, but can use serial PCT to guide antibiotic discontinuation
- Not severely immunocompromised (other than corticosteroids)^a
- No other concomitant infection requiring antibiotics



SUSPECTED SEPSIS IN CRITICALLY ILL PATIENT

- Not severely immunocompromised (other than corticosteroids)^a
- Not on antibiotics for chronic bacterial infection (e.g., endocarditis, osteomyelitis)



^a“Severely immunocompromising conditions” include bone marrow transplantation, solid organ transplantation, chemotherapy-induced neutropenia with ANC <500, and advanced HIV/AIDS. Pregnancy and cystic fibrosis have also typically been used as exclusion criteria in PCT trials.

^b Certain infections require a prolonged duration of antibiotics even if PCT levels decrease to \leq 0.5, including *Staphylococcus aureus* bacteremia, endocarditis, osteomyelitis, joint infections, mediastinitis, liver/brain abscesses, and chronic prostatitis.

Additional Notes:

- If PCT levels do not decline despite therapy, consider treatment failure (e.g., inadequate antibiotic therapy or source control).
- False positives can occur from noninfectious conditions that cause systemic inflammation, such as severe trauma, circulatory shock, major surgery, burns, inhalation injury, and pancreatitis.
- False negatives can occur early in the course of disease, or in contained localized infections (e.g. mediastinitis, empyema, abscesses).
- PCT algorithms can be used as a clinical decision aid but should never override clinical judgment.

Suggested Algorithm for PCT Use at BWH, Cont'd

Caveats and Limitations of PCT:

- 1. False positives can occur.** Major stressors that cause systemic inflammation, such as severe trauma, circulatory shock, surgery, burns, inhalation injury, and pancreatitis can also cause elevations in PCT. PCT can also be elevated in neonates (immediately following birth), after receipt of certain immunotherapy agents (e.g., granulocyte transfusions, antilymphocyte globulin, anti-CD3 antibodies), malaria, some fungal infections, medullary thyroid tumors, and end-stage renal disease (if not yet on hemodialysis).
- 2. False negatives can also occur.** False negatives can also occur, notably in contained localized infections such as mediastinitis, empyema, or abscesses, or if PCT is drawn too early in the course of infection. If a low PCT level is used to support the decision to withhold antibiotic therapy in a hospitalized patient, a repeat PCT level within 6-24 hours is therefore recommended.
- 3. Severely immunocompromised patients have been excluded from virtually all procalcitonin trials.** “Severely immunocompromised” has not always been well-defined in the PCT trials, but we suggest the following criteria: a) bone marrow transplant, b) solid organ transplant, c) chemotherapy-induced neutropenia with absolute neutrophil count <500, and d) advanced HIV/AIDS. Because of the relative lack of data, we advise that PCT levels not be drawn in these patients; if drawn, extra caution should be taken when using PCT to guide clinical decision-making. Of note, corticosteroid use alone has NOT typically been used as exclusion criteria. **Other conditions that have been typically been used as exclusion criteria from PCT trials include pregnancy, cystic fibrosis, and infections that clearly need prolonged antibiotic therapy (such as osteomyelitis or endocarditis).**
- 4. Procalcitonin should never override clinical judgment.** In most of the PCT trials, over-ruling of PCT algorithms was allowed and in fact common in the ICU-based studies (50% of more), underscoring the fact that PCT should be used as an adjunct to clinical judgement rather than a replacement. Many of our hospitalized patients have complex histories, comorbidities, and clinical presentations and thus the presence of infection cannot be definitely determined by a single lab test.