



Community-Acquired Pneumonia for the Hospitalist: Updates and Controversies

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Abstract

The American Thoracic Society (ATS)/Infectious Disease Society of American (IDSA) guidelines for the diagnosis and treatment of community-acquired pneumonia (CAP) were released in 2019. While most categories had minor updates, one major change was abandonment of the term “healthcare-associated pneumonia” (HCAP). The guidelines also recommended against use of procalcitonin for the decision to initiate antibiotics; recommended against use of corticosteroids in all cases but pneumonia with septic shock; and recommended obtaining blood and sputum cultures in patients with pneumonia at risk for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*. This review will cover studies published since the 2019 guidelines that help answer unaddressed questions and/or add clarity to areas of uncertainty.

Ms. S is an 82-year-old with mild dementia and insulin-dependent diabetes, who came to the Emergency Department from her skilled nursing facility for worsening confusion, 2-3 days of cough productive of purulent sputum, and fevers to 101.5° F. Vital signs are notable for a respiratory rate of 24 breaths/minute and oxygen saturation of 92% on room air. Her labs are significant for blood urea nitrogen of 29 mg/dL and creatinine of 1.4 mg/dL, which is new. She has a leukocytosis of 15,000/mcL. Her chest X-ray (CXR) is read as “bibasilar opacities, possible atelectasis versus infection, correlate clinically”.

The American Thoracic Society (ATS)/Infectious Disease Society of American (IDSA) guidelines for the diagnosis and treatment of community-acquired pneumonia (CAP) were released in 2019.¹ While most categories had minor updates, one major change was abandonment of the term “healthcare-associated pneumonia” (HCAP). The guidelines also recommended against use of procalcitonin for the decision to initiate antibiotics; recommended against use of corticosteroids in all cases but pneumonia with septic shock; and recommended obtaining blood and sputum cultures in patients with pneumonia at risk for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*. This review will cover studies published since the 2019 guidelines that help answer unaddressed questions and/or add clarity to areas of uncertainty.

HOW SHOULD WE DIAGNOSE PNEUMONIA IN PATIENTS WITH EQUIVOCAL CXRS?

The 2019 IDSA/ATS guidelines focused only on patients who met radiographic criteria for pneumonia¹ and do not provide guidance for indeterminate cases, such as when patients have clinical signs and symptoms of pneumonia, but have a negative CXR.

While there is no gold standard for pneumonia diagnosis, chest computed tomography (CT) detects more cases of pneumonia than CXR. However, indiscriminate use of CTs exposes patients to radiation and potentially increases incidental findings—and costs and patient anxiety.^{2,3} CTs are thus best used in cases of intermediate probability, e.g., when CXR and signs/symptoms are discordant.³ Loubet et al. created a 2-step diagnostic algorithm using a predictive score combining clinical symptoms, CXR findings, C-reactive protein (CRP) levels, and versions with and without multiplex PCR testing results. Only patients with mid-range scores underwent further testing with lung CT. Of 319 patients, 55% underwent CT scanning and 45% had the pre-test probability of CAP modified.⁴ The authors did not indicate whether the modified probability changed patient treatment. Whether CT scanning changes antibiotic use is still to be determined.

Point-of-care lung ultrasound (LUS), an emerging method of diagnosing pneumonia, is superior to CXR. Unlike chest CT, ultrasound does not expose the patient to radiation and can be used to quickly assess the patient and provide information in real time. LUS has a sensitiv-

ity and specificity equal to that of CT, especially when LUS protocols are combined to maximize ability to either detect pneumonia or rule it out.⁵ While training is required, protocols such as the bedside lung ultrasound examination (BLUE) and the fluid limited by lung sonography (FALLS) protocols were designed to be minimally operator-dependent⁶; basic competence of other protocols can be achieved in as few as 25 supervised exams.⁷ Like lung CT, LUS can be combined with other diagnostic modalities to increase sensitivity/specificity. Bessat et al. concluded that an algorithm incorporating procalcitonin with LUS improved diagnostic accuracy, although no trials have yet evaluated impact on antibiotic use.⁸

Molecular assay/multiplex PCR is increasingly being used both in diagnosis of CAP as well as in determining etiology. In a study involving 737 patients, molecular testing of good quality sputum samples demonstrated a negative predictive value (NPV) of 92-100%.⁹ The positive predictive value (PPV) was extremely variable (5%-100%), suggesting that positive results should be treated with caution. Many patients presenting with respiratory illness are unable to produce a good quality sputum sample; a small study comparing the results of molecular testing on oropharyngeal swab samples with results of sputum samples (88% of which were induced) found a high negative percent agreement (90-100%) and a high presumed NPV (0.91 – 1).¹⁰ As with the previous study, the positive percent agreement and PPV was variable (0-100% and 0.09 – 1, respectively), with greater agreement seen in more common pathogens. These findings suggest that oropharyngeal swabs may be useful to rule out pneumonia for patients who are unable to produce sputum. Molecular assays show great promise as results are available rapidly, they are possibly less affected by antibiotic use, and they provide information about many antibiotic resistance genes. Although there is start-up cost associated with testing, one small study involving patients hospitalized in the intensive care unit found that overall costs were minimal given cost savings from antimicrobial stewardship.¹¹ Given the variable PPV seen in most studies, clinicians should interpret positive results with caution, although the PPV may be improved by combining molecular assays with other tools. One study is currently underway to examine the utility of combining molecular assay testing with procalcitonin.¹² Clinicians should be aware that not all bacteria are represented on available commercial tests and that most studies have been performed with patients who were able to produce good quality sputum samples. It is unclear how quality of sputum impacts the NPV.

HOW SHOULD WE SELECT ANTIBIOTICS?

The 2019 ATS/IDSA guidelines recommend either a respiratory fluoroquinolone or a β -lactam / macrolide combination as first-line therapies for mild-to-moderate un-

complicated CAP and a β -lactam / doxycycline combination as a second-line option for patients with a contraindication to fluoroquinolones and macrolides and if the patient is not at risk for *Legionella longbeachae*.¹ Levofloxacin has higher cure rates than β -lactam / macrolide combinations but does not have a mortality benefit and is associated with aortic dissections and tendon injuries for those at increased risk, which includes elderly patients.^{13,14} Azithromycin is associated with fatal arrhythmias, particularly in patients with prolonged QT intervals.¹⁵ Doxycycline-containing regimens may be associated with a decreased risk of *Clostridium difficile* infection compared to other regimens^{16,17}; however, there is no recent data comparing the efficacy of doxycycline to that of levofloxacin or a β -lactam / macrolide combination and it therefore remains a second-line therapeutic option.¹ While a 2023 meta-analysis found doxycycline monotherapy was comparable to fluoroquinolone or macrolide monotherapies in mild-to-moderate CAP, the most recent trial included was from 2004.¹⁸ Severe CAP should be treated with a β -lactam / macrolide combination or a β -lactam / respiratory fluoroquinolone if the patient has a contraindication to macrolides.¹

One of the most notable changes in the 2019 ATS/IDSA guidelines was deletion of the term “HCAP” .¹ Instead, the guidelines suggest that empiric therapy directed towards MRSA and *P. aeruginosa* should be given to patients who have been hospitalized within 90 days and have received parenteral antibiotics, or have had previous infection with MRSA or *P. aeruginosa* (or other drug-resistant pathogens [DRPs]). The guidelines state that clinicians should use “local risk factors” as guidance. This recommendation has left many clinicians in search of additional guidance.

There have been several clinical-prediction models that have attempted to further define which patient populations are at risk for DRPs; Gil and Webb provide an overview of available prediction models.¹⁹ In a study involving several hospitals in the United States, use of the “Drug Resistance in Pneumonia (DRIP)” score safely reduced antipseudomonal antibiotic use by 8.9% and, when combined with an MRSA nasal swab, reduced vancomycin use by 16.9%.²⁰ Regardless, no single clinical prediction model has been shown to consistently outperform HCAP criteria in all settings. Gil and Webb recommend that clinicians should compare the performance of clinical prediction models against local resistance patterns before incorporating models into routine practice.¹⁹ The severity of illness and risk of inadequate therapy should also be considered when selecting empiric therapy for those at risk for DRP infection.¹⁹ If a patient is determined to be at risk for DRPs through use of a model, clinicians should look for recent respiratory culture data and make an effort to obtain current culture data so that antibiotic therapy can be de-escalated.^{19,21} If available,

molecular testing can provide additional helpful data, with the caveats mentioned earlier.

SHOULD WE ADD CORTICOSTEROIDS IN CASES OF SEVERE COMMUNITY ACQUIRED PNEUMONIA?

Whether or not to use corticosteroids in the treatment of CAP has remained an area of controversy, with the 2019 ATS/IDSA guidelines recommending corticosteroid use only in patients with septic shock.¹ Since 2019, several meta-analyses have been performed, with mixed conclusions about the impact of corticosteroids on mortality and other outcomes. The results of two major new studies were released in March and October of 2023 which provide further evidence of benefit of corticosteroid use in patients with severe CAP. The first is a randomized, controlled trial of 800 patients with severe CAP who were randomized to either intravenous hydrocortisone (200 mg continuous infusion for 4-7 days followed by an 8-14 day taper) or placebo.²² The authors found a significantly lower mortality rate at 28 days and 90 days for the patients that received hydrocortisone. Hyperglycemia was more common in patients treated with hydrocortisone, but there was no difference in other adverse events. The second study is a meta-analysis that included 15 randomized, controlled trials and 3367 patients. Nine of the trials included patients with severe CAP. The authors found a significant reduction in all-cause mortality and acute respiratory distress syndrome (ARDS) in patients treated with corticosteroids, which was most pronounced in patients with severe CAP. There was an increase in hyperglycemia but no other difference in adverse events, including secondary infections, gastrointestinal bleeding, and hospital readmissions.²³ Significant heterogeneity between corticosteroids and dosing precluded the authors from making recommendations on corticosteroid type and dosing schedule, however the authors of the randomized controlled trial point out that most trials demonstrating a mortality benefit used hydrocortisone.²² Until further studies define which patients benefit from corticosteroids (and from which corticosteroid/which dose), hydrocortisone should be considered in patients with severe CAP, given the potential mortality benefit and the relatively low risk of treatment.

DOES PROCALCITONIN HAVE A ROLE IN THE DIAGNOSIS OR TREATMENT OF PNEUMONIA?

Procalcitonin is typically used by clinicians in (a) determining whether a pneumonia is present and whether antibiotics should be prescribed; (b) determining whether a bacterial pneumonia is superimposed on a viral pneumonia; or (c) determining whether antibiotics can be

stopped. The 2019 ATS/IDSA guidelines recommended against its use in determining whether antibiotics should be initiated.¹ There are several studies that suggest that procalcitonin is neither specific nor sensitive enough to use in the decision to withhold or start antibiotics in the hospital setting. A recent meta-analysis incorporating 12 studies and 2408 patients with confirmed etiologies for CAP found a pooled sensitivity of 0.55 and a specificity of 0.76, when using the most commonly used procalcitonin cut-point of 0.5 microgram/L.²⁴ Several studies have demonstrated that procalcitonin algorithms can be used to reduce antibiotic days and used in antimicrobial stewardship efforts, particularly in patients with COVID-19.^{25,26} However, no studies have demonstrated a reduction in antibiotic days for hospitalized patients diagnosed with CAP beyond what is currently recommended in the 2019 ATS/IDSA guidelines. Therefore, procalcitonin is not likely to be useful as a sole indicator in the decision to initiate antibiotics in patients with CAP requiring hospitalization and has not been shown to be useful to reduce antibiotics for less than 5 days (the currently recommended duration). Procalcitonin may be useful combined with other diagnostic modalities, such as ultrasound⁸ or molecular testing,¹² although more clinical trials are needed in these areas.

KEY TAKEAWAYS

- Available modalities to diagnose pneumonia in patients with equivocal CXRs, include lung CT, LUS, and molecular assays. The choice of test should be driven by availability and then by cost and exposure to radiation.
- Several clinical-prediction models have attempted to further define which patient populations are at risk for DRPs but no single clinical prediction model has been shown to consistently outperform HCAP criteria in all settings. Clinicians should use the tool that best reflects the local resistance patterns and follow up with further microbiological testing.
- Until studies are available that further define which patients benefit from corticosteroids (and from which corticosteroid/which dose), hydrocortisone should be considered in patients with severe CAP, given the mortality benefit and the relatively low risk of treatment.
- Several studies suggest that procalcitonin is neither specific nor sensitive enough to use in the decision to withhold or start antibiotics in the hospital setting. Procalcitonin may be useful in conjunction with other diagnostic modalities but should not be used as a sole driver of clinical decision making.

DISCLOSURES / CONFLICTS OF INTEREST

None

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