Long-Term Care Updates

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Update on the Treatment of Community Acquired Pneumonia in Adults

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Community Acquired Pneumonia

Community acquired pneumonia (CAP) is defined as an acute infection of the lung parenchyma acquired outside of the hospital setting. It can be caused by a variety of microorganisms, including both bacteria and viruses.[1] In 2017, influenza and pneumonia, combined, ranked as the 8th leading cause of death in the United States.[2] The incidence of CAP increases with age, and risk is higher in patients with chronic comorbidities such as chronic lung, renal, heart, and liver disease; diabetes; patients taking opioids or proton pump inhibitors; and those who smoke or have a high alcohol intake.[3]

Guidelines for the Treatment of CAP

The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) published updated guidelines for the management of CAP in adults in October 2019.[4] Several recommendations remained unchanged; however, there were some notable updates. The key difference between the two sets of guidelines is the recommendation for more microscopic testing of respiratory tract samples in an effort to reduce prescribing medications for drug-resistant bacteria when not necessary.[5]

Whereas the previously published guidelines recommended sputum and blood cultures only in patients with severe disease,[6] the new recommendation is to obtain both in all patients with severe disease, as well as inpatients empirically treated for methicillin-resistant *Staphylococcus aureus* (MRSA) or *Pseudomonas aeruginosa*.[4] It is not recommended to use a serum procalcitonin level to guide therapy choice. Additionally, there have been updates to initial treatment strategies. The Table on the next page outlines recommendations for empiric therapy in outpatient and inpatient settings. The new guidelines state that until microbiological testing is fast, accurate, and affordable, most treatment for patients with CAP will remain empiric.[4] However, if a causative pathogen is identified, treatment should be directed at the specific pathogen.

Table. Initial Treatment of CAP in Adults[4]

Outpatient Treatment	
Patient Factors	**Recommendation**
No Comorbidities or Risk Factors for MRSA or *Pseudomonas aeruginosa*	Amoxicillin OR Doxycycline OR Macrolide (azithromycin, clarithromycin, clarithromycin ER) if local pneumococcal resistance is <25%
Presence of Comorbidities (chronic heart, liver, lung, or renal disease; diabetes; alcoholism; malignancy; or asplenia)	<u>Combination Therapy:</u> Amoxicillin/clavulanate or cephalosporin (cefpodoxime, cefuroxime) AND Macrolide (azithromycin, clarithromycin, clarithromycin ER) or doxycycline
	<u>Monotherapy:</u> Respiratory fluoroquinolone (levofloxacin, moxifloxacin, gemifloxacin)
Inpatient Treatment	
Patient Factors	**Recommendation for Standard Regimen†**
Non-Severe Pneumonia	Beta-lactam (ampicillin/sulbactam, cefotaxime, ceftriaxone, ceftaroline) and macrolide (azithromycin, clarithromycin) OR Respiratory fluoroquinolone (levofloxacin or moxifloxacin)
Severe Pneumonia	Beta-lactam (ampicillin/sulbactam, cefotaxime, ceftriaxone, ceftaroline) and macrolide (azithromycin, clarithromycin) OR Beta-lactam (ampicillin/sulbactam, cefotaxime, ceftriaxone, ceftaroline) and fluoroquinolone (levofloxacin or moxifloxacin)

†Additional recommendations exist in cases of prior respiratory isolation of MRSA or *Pseudomonas aeruginosa* or recent hospitalization with parenteral antibiotics and locally validated risk factors for MRSA or *Pseudomonas aeruginosa*.

The previously published guidelines for the management of CAP in adults referred to "healthcare-associated pneumonia". This term was used for nonambulatory patients with pneumonia who were residents of nursing homes or other long-term care facilities. These patients received a separate designation due to their potential risk for antibiotic-resistant pathogens. The previous recommendation was to treat many of these patients the same as those with hospital-acquired pneumonia.[6] However, the updated guidelines eliminated this term and suggest that these patients be treated using the CAP treatment recommendations, and only covering empirically for MRSA or *Pseudomonas aeruginosa* if there are locally validated risk factors present.[4]

Finally, although the 2007 guidelines did not address the use of corticosteroids, the new guidelines do not recommend routine use of these agents in patients with either non-severe or severe disease. The authors cite a lack of evidence demonstrating benefit in non-severe CAP and limited evidence in severe CAP. However, corticosteroids may still be appropriate in patients with comorbid diseases, such as chronic obstructive pulmonary disease, asthma, and autoimmune disease.[4]

Lefamulin: A New Option for the Treatment of CAP

Lefamulin is a first-in-class semisynthetic pleuromutilin antibiotic available in oral and injectable formulations that was approved in August 2019.[7-10] It is indicated for the treatment of adults with community-acquired bacterial pneumonia (CABP) caused by the following susceptible microorganisms: *Streptococcus pneumoniae*, *Staphylococcus aureus* (methicillin-susceptible isolates), *Haemophilus influenzae*, *Legionella pneumophila*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae*.[7] Lefamulin has a unique mechanism of action: bacterial synthesis is inhibited through hydrogen bonds, hydrophobic interactions, and Van der Waals forces, which prevents the positioning of tRNA.[8,9] Its mechanism of action results in a lower chance of cross-resistance to other antibiotic classes.[11] Depending on the bacterial organism, lefamulin may be bactericidal (*S. pneumoniae*, *H. influenzae*, and *M. pneumoniae*) or bacteriostatic (*S. aureus* and *S. pyogenes*).[8]

Although lefamulin is not included as a first-line agent in the updated ATS/IDSA guidelines, it is anticipated that its use would be after microbiological testing. The prescribing information states that lefamulin should only be used when susceptible bacteria are proven or strongly suspected as the cause of infection in order to reduce antibiotic resistance.[7] The Lefamulin Evaluation Against Pneumonia (LEAP) 1 trial suggested that lefamulin is an effective empiric monotherapy option in the treatment of CABP[12] but the authors of the ATS/IDSA guidelines concluded that there is a need for further high-quality research with lefamulin to validate its use in the outpatient and hospital settings.[4]

Summary

New guidelines based on updated data are available to assist providers in treating CAP in adults. These guidelines suggest more microscopic testing of respiratory tract samples in an effort to reduce prescribing medications for drug-resistant bacteria when not necessary. The authors noted their disappointment in the lack of data available to make strong recommendations regarding the standard of care in CAP therapy. They recognize the need for further investigation to address knowledge gaps. Lefamulin is a new, first-in-class semisynthetic pleuromutilin antibiotic available in oral and injectable formulations for the treatment of CABP. It is not included as a preferred agent in the updated guidelines, but it is anticipated that its use would be after microbiological testing. There is a need for further high-quality research with lefamulin to validate its use in the outpatient and hospital settings.

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