Community-Acquired Pneumonia – Frequently Asked Questions

In outpatient CAP in healthy patients without comorbidities, why are azithromycin and doxycycline monotherapy no longer recommended?

Per the 2019 SHC Antibiogram, macrolide and tetracycline resistance in S. pneumoniae is 44% and 42%, respectively. Negative clinical outcomes like breakthrough bacteremia have been shown in patients with erythromycin-resistant pneumococcal pneumonia receiving macrolide therapy. The 2019 ATS/IDSA CAP Guidelines recommend avoidance of macrolide monotherapy when local pneumococcal resistance rates exceed 25%. While the guidelines do not address a local threshold for S. pneumoniae tetracycline (doxycycline) resistance directly, the SHC resistance rate (42%) varies so substantially from the 2017 U.S. national average (11%) that an empiric recommendation cannot be justified.

In outpatient CAP in healthy patients without comorbidities, why is amoxicillin monotherapy recommended, which does not have “atypical” coverage?

Multiple prospective, randomized studies have demonstrated equivalent efficacy of high dose amoxicillin to antimicrobials with atypical coverage including fluoroquinolones and ketolides in patients with CAP. Meta-analyses of these and other studies comparing beta lactams with macrolides or fluoroquinolones also demonstrated no differences in clinical success and mortality, particularly in healthy outpatients with CAP. Additionally, per the 2018 SHC Antibiogram, using penicillin as a surrogate, amoxicillin susceptibility amongst S. pneumoniae is very high at 98%.

Why is Healthcare Associated Pneumonia (HCAP) no longer a recognized clinical entity?

The term ‘HCAP’ was initially coined based on studies showing a higher prevalence of organisms like MRSA and P. aeruginosa in certain subsets of patient with CAP (e.g. dialysis, nursing home residence, recent hospitalization, home infusion therapy, home wound care). In prior pneumonia guidelines, broader spectrum therapy was recommended in patients who met any of these HCAP criteria. However, more recent meta-analyses of subsequent studies showed poor discriminatory ability of the HCAP criteria to detect MRSA and P. aeruginosa, no increase in mortality of HCAP, and significant publication bias and low study quality. Numerous studies have also shown no difference in outcomes when using standard CAP therapy compared with broader spectrum therapy with anti-pseudomonal and MRSA activity in aggregate, as well as subsets of non-severe disease or non-ICU patients and critically ill patients. See below for when empiric MRSA or P. aeruginosa-directed therapy should be considered.

What is the evidence behind when empiric MRSA or Pseudomonas coverage should be considered?

Overall, incidence of MRSA and P. aeruginosa in CAP is low. The strongest predictor of MRSA or P. aeruginosa is prior isolation of these organisms from respiratory culture. The 2019 ATS/IDSA CAP guidelines recommend empirically covering MRSA or P. aeruginosa, respectively, if these organisms...
have been isolated from respiratory cultures in the past 12 months. Receipt of broad spectrum intravenous antibiotics during hospitalization was also identified as a predictor of MRSA and \textit{P. aeruginosa} but its association is weaker, thus the 2019 ATS/IDSA CAP guidelines recommend only empirically covering these organisms in severe CAP, otherwise respiratory cultures should be obtained and MRSA or \textit{P. aeruginosa} coverage added only if these organisms are isolated. Other less strongly associated risk factors for MRSA include recurrent skin infections and severe disease. For \textit{P. aeruginosa} they include tracheostomy, bronchiectasis, severe COPD, and invasive respiratory or vasopressor support. If antimicrobials for MRSA and/or \textit{P. aeruginosa} are initiated, blood and respiratory cultures as well as nasal MRSA PCR screen should be performed and if these assays do not identify these pathogens, therapy can be narrowed.

**Why do patients with suspected aspiration pneumonia (without radiographic evidence of lung abscess or empyema) no longer need additional anaerobic coverage?**

While more definitive research is needed in this area, the origins of needing anaerobic coverage (e.g. adding metronidazole) were based on studies of aspiration pneumonia using trans-tracheal aspiration in patients late in their disease course finding high rates of anaerobic organisms. More recent studies have found that gram negative aerobic organisms are more common and anaerobes play less of a role. Additionally, what may initially be diagnosed as aspiration pneumonia could instead be aspiration pneumonitis, a non-infectious syndrome, in which patients improve rapidly and antimicrobials do not affect outcome. Thus, the 2019 ATS/IDSA CAP Guidelines do not recommend adding anaerobic coverage for aspiration pneumonia unless radiographic evidence of lung abscess or empyema exist.

**When discharging a patient with CAP, given potential insurance formulary challenges, can other cephalosporins like cefdinir or cefixime be substituted?**

The 2019 ATS/IDSA CAP Guidelines only recommend cefpodoxime and cefuroxime as oral cephalosporin options in the treatment of CAP along with amoxicillin/clavulanate. Cefdinir does carry an FDA indication for CAP and its use is supported by a prospective randomized controlled trial at a dosage of 300 mg PO BID, where it achieved 89% clinical cure. While inclusion criteria were not as stringent as modern CAP trials and duration of therapy was 10 days, on subgroup analysis, cefdinir did demonstrate high cure rates (85-100%) in culture-positive pneumonia with \textit{S. pneumoniae}, \textit{M. catarrhalis}, \textit{H. influenzae}, and \textit{H. parainfluenzae} supporting its efficacy. Cefixime is another commonly used oral 3rd generation cephalosporin, however, it does not carry an FDA indication for pneumonia and clinical studies supporting its use are of poor quality.

**What is the appropriate treatment duration of CAP?**

Several randomized controlled trials have demonstrated similar efficacy with 5 days (or less) of antibiotic therapy to longer courses (8-10 days). The 2019 ATS/IDSA CAP Guidelines recommend that in patients with CAP with clinical improvement (i.e. resolution of vital sign abnormalities, normal
mentation, ability to eat), treatment should be no less than 5 days. In patients who do not stabilize by day 5 of treatment should be evaluated for drug-resistant pathogens, complications of pneumonia, or other sources of infection/inflammatory response. Duration of therapy should be extended to 7 days in patients with documented MRSA or *P. aeruginosa* pneumonia and duration should be extended appropriately if pneumonia is complicated by meningitis, endocarditis, or other deep-seated infection or caused by other less common pathogens (e.g. *M tuberculosis* or endemic fungi).

**Can azithromycin be discontinued after 3 days of therapy at 500 mg daily?**

Multiple randomized studies of atypical pneumonia and CAP, demonstrated similar treatment efficacy between 3 days of azithromycin (500 mg PO daily) compared with both 5 days of azithromycin (500 mg PO on day 1 followed by 250 mg PO on days 2-5) and 8 days of clarithromycin. In patients with CAP and rapid clinical improvement on therapy with a beta lactam and azithromycin 500 mg daily, azithromycin can be safety discontinued after 3 doses, while the beta lactam can be continued for at least 5 total days of therapy as above.


