



# When to “CAP” off treatment for pneumonia

## Is 5 days of antibiotic therapy really sufficient for adults hospitalized with community-acquired pneumonia?

### PRACTICE CHANGER

Prescribe 5 days of antibiotic treatment for inpatients with community-acquired pneumonia because it produces the same clinical success rates as longer treatment regimens, but is associated with fewer negative patient outcomes.<sup>1</sup>

### STRENGTH OF RECOMMENDATION

**B:** Based on a single, good-quality randomized control trial.

Uranga A, España PP, Bilbao A, et al. Duration of antibiotic treatment in community-acquired pneumonia: a multicenter randomized clinical trial. *JAMA Intern Med.* 2016;176:1257-1265.<sup>1</sup>

### ILLUSTRATIVE CASE

A 65-year-old woman is admitted to your inpatient service from your family health center. She is diagnosed with community-acquired pneumonia (CAP) based on a 5-day history of cough and fever and a positive chest x-ray. She now requires oxygen at rest. She has a past medical history of hypertension and diabetes, both of which have been controlled on oral medications. Antibiotic therapy is initiated for the treatment of the pneumonia, but what treatment duration is ideal?

The World Health Organization estimates that pneumonia is the third most common cause of mortality worldwide, causing 3.2 million deaths per year.<sup>2</sup> Appropriate prescribing of antibiotics is critical for the successful treatment of CAP.

The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) created consensus guidelines,

published in 2007, for the treatment of CAP.<sup>3</sup> These guidelines recommend a minimum 5-day course of antibiotics if the patient is clinically stable, which is defined as: afebrile for 48 hours, heart rate  $\leq 100$  beats/minute, respiratory rate  $\leq 24$  respirations/minute, systolic blood pressure  $\geq 90$  mm Hg, oxygen saturation  $\geq 90\%$ , normal mental status, and able to tolerate oral intake. Longer antibiotic treatment durations are recommended on an individualized basis, if, for example, the isolated pathogen is not susceptible to the initial antibiotic or if the infection was caused by an extrapulmonary source.

However, these recommendations are not routinely followed. Practitioners often make it their custom to prescribe longer courses of antibiotics.<sup>4</sup> And yet we know that there are several reasons to consider shorter courses of antibiotics, including lower health care costs, fewer adverse effects, and lower rates of bacterial resistance.<sup>5-7</sup>

■ **Two meta-analyses were performed** to compare the safety and efficacy of short- ( $\leq 7$  days) vs long-course ( $> 7$  days) antibiotic therapy in CAP.<sup>8,9</sup> Both meta-analyses found no difference in efficacy or safety between shorter and longer courses of antibiotic treatment regimens for CAP. Secondary outcomes noted a trend toward decreased antibiotic-associated adverse events with shorter courses of therapy.<sup>8,9</sup>

While these meta-analyses supported shorter courses of antibiotics for CAP, there are limitations to the broad implementation of their findings. Studies included in these analyses utilized a variety of antibi-

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➤ This is the first study to support the efficacy of the 5-day course of antibiotics for hospitalized CAP patients recommended by IDSA/ATS guidelines.

otic treatment regimens and longer courses (7 days vs 5 days) that are not recommended by the IDSA/ATS guidelines. Additionally, studies included both inpatient and outpatient treatment groups, so findings may not apply to an exclusively inpatient CAP population.<sup>8,9</sup>

This study sought to validate the IDSA/ATS guidelines recommending a 5-day course of antibiotics for hospitalized patients with CAP.<sup>1</sup>

#### STUDY SUMMARY

##### No differences in clinical outcomes between 5 days of Tx—and longer

This multicenter, double-blind, noninferiority randomized trial compared short-term antibiotic treatment duration (5 days) to physician-discretion antibiotic treatment duration among 312 patients  $\geq 18$  years of age admitted for CAP to one of 4 teaching hospitals in Spain.<sup>1</sup> Pneumonia was diagnosed on chest radiograph with at least one symptom: cough, fever, dyspnea, or chest pain. Patients were excluded if, among other things, they had an immunocompromising condition, lived in a nursing home, had a recent hospital stay, used antibiotics within the previous 30 days, or had an uncommon pathogen, such as *Pseudomonas aeruginosa* or *Staphylococcus aureus*.<sup>1</sup>

Patients were randomized after receiving a minimum of 5 days of antibiotics to an intervention group (where, if clinically stable, no further antibiotics were given) or a control group (where physicians determined antibiotic duration).<sup>1</sup> Primary outcomes were clinical success rate at Days 10 and 30 from admission, defined as resolution of signs and symptoms of CAP without further antibiotics, and improvement of CAP-related symptoms as determined by an 18-item CAP symptom questionnaire. This questionnaire was scored 0 to 90, where higher scores indicated greater severity. Secondary outcomes included: duration of antibiotic use, time to clinical improvement, mortality, hospital readmission, hospital length of stay, and CAP recurrence.<sup>1</sup>

A total of 312 patients were randomized with 162 patients in the intervention group and 150 patients in the control

group. The mean age of patients in the intervention and control groups was 66.2 and 64.7 years, respectively. Other baseline demographics were similar between the groups. Nearly 80% of patients received quinolone treatment; <10% received a beta-lactam plus a macrolide.<sup>1</sup>

Clinical success rates were similar for the control and intervention groups, respectively, at Day 10 (49% vs 56%;  $P=.18$ ) and Day 30 (89% vs 92%;  $P=.33$ ). There was shorter median treatment duration with antibiotics in the intervention group compared with the control group (5 days vs 10 days;  $P<.001$ ) and fewer 30-day hospital readmissions (1.4% vs 6.6%;  $P=.02$ ). There were no differences for other secondary outcomes.<sup>1</sup>

#### WHAT'S NEW

##### Clinical support for 2007 guidelines

This is the first study to clinically support the IDSA/ATS guidelines, which state that a 5-day course of antibiotic therapy for hospitalized adults with CAP is effective and without increased risk of adverse events.

#### CAVEATS

##### Generalizability to other meds and settings is unclear

This study focused on antibiotic duration for the treatment of CAP in hospitalized patients and mainly used quinolone antibiotics. It remains unclear if duration of therapy is as effective in the outpatient setting or when using alternative antibiotic regimens.

If patients continued to have symptoms (such as fever or low oxygen saturation on room air) after 5 days of antibiotic treatment, antibiotic treatment was continued in the study. Thus, patients in real life who continue to have symptoms may need individualized therapy and may require more than 5 days of antibiotics.

#### CHALLENGES TO IMPLEMENTATION

##### Antibiotics end before clinical improvement occurs

This study noted an average of 12 days in both groups for patients to achieve clinical

improvement, with upwards of 15 to 18 days for patients to return to normal activity. Patients and providers may be dissatisfied if the treatment course ends days before clinical improvement of symptoms. This may cause prescribers to lengthen the duration of antibiotic therapy inappropriately. **JFP**

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