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The Maturing Antibiotic Mantra: "Shorter Is Still Better"

Brad Spellberg, MD[1,2,*]

[1]Los Angeles County + University of Southern California (LAC+USC) Medical Center, Los Angeles, California

[2]Division of Infectious Diseases, Keck School of Medicine at USC, University of Southern California, Los Angeles, California.

The proper duration of antibiotic therapy for various infections is a matter of long-standing consternation. For decades, the standard antibiotic course for most acute bacterial infections has been 7 to 14 days, based largely on the fact that the week has 7 days in it.[1] The reason the week has 7 days in it dates back to an edict issued by Constantine the Great in 321 AD.[1] To underscore the absurdity of basing 21st century antibiotic course durations on an ancient Roman Emperor's decree, I refer to such durations as "Constantine Units." One Constantine Unit is a 7-day course of antibiotics, and 2 Constantine Units is a 14-day course.

It has been nearly 10 years since Dr. Lou Rice first publicly called out the need to move to shorter courses of antibiotic therapy based on high-quality data.[2] Nearly 5 years ago, colleagues picked up Dr. Rice's mantle and again called for the medical community to move to short-course antibiotic therapies.[3] There have been dozens of antibiotic trials comparing shorter versus longer durations of therapy for a variety of acute bacterial infections (Table).[1] Essentially, all such trials studying acute bacterial infections in adults have found that shorter-course therapy is just as effective as longer therapy.

Based on such a plethora of data, a year ago, I suggested that physicians replace the dogma of Constantine-Unit-based durations of therapy with a new mantra, "shorter is better."[1] A year later, that mantra is no longer new. It is maturing, but it is not yet sufficiently widespread among providers. As a result, providers continue to prescribe unnecessarily long durations of antibiotic therapy, which wastes antibiotics, results in increased selective pressure driving antibiotic resistance, and continues to erode the miraculous efficacy of these drugs.

Royer et al.[4] have now added to the overwhelming evidence in favor of short-course antibiotic therapy with a new meta-analysis comparing shorter courses with longer courses of therapy for acute bacterial infections, specifically for hospitalized patients. They studied clinical trials comparing shorter versus longer courses of therapy for hospital inpatients with pneumonia, complicated urinary tract infections, intraabdominal infections, or nosocomial infections of unknown origin. Across 13 clinical trials that included efficacy data, cumulatively, the investigators found no difference in clinical cure, microbiological cure,

[*]**Address for correspondence:** Brad Spellberg, MD, 2051 Marengo Street, Los Angeles, CA 90033; Telephone: 323-409-6734; bspellberg@dhs.lacounty.gov.

mortality, or infection relapses between short courses and longer courses of therapy. As mentioned, this result is concordant with an extensive body of literature on this topic (Table).

The fact that short durations of antibiotics can cure infections has been known for a long time. In the early penicillin era, courses of therapy were typically 1 to 4 days with good success rates.[2] Interestingly, in a recent clinical trial in which daptomycin was found to be ineffective for community-acquired pneumonia (because of inactivation by pulmonary surfactant), a single dose of ceftriaxone markedly improved the cure rate for pneumonia in the daptomycin arm.[5,6] The salutary effect of a single dose of ceftriaxone on the clinical cure for pneumonia reinforces how badly we have been overtreating infections for many years.

Many of the signs and symptoms of bacterial infections result from the inflammatory response to the bacteria rather than the direct presence of viable bacteria. Thus, the persistence of symptoms for a few days does not necessarily mean that viable bacteria are still present (ie, symptoms can persist even when all the bacteria are dead). It is likely that a reasonable proportion of patients with acute bacterial infections are cured with 1 day of therapy, and that additional days are decremental to increasing that cure rate. Even 5 days of antibiotics are likely more than is needed to cure the large majority of patients with acute bacterial infections.

Unfortunately, we do not yet have the technology to truly customize durations of therapy in individual patients, although the resolution of high-procalcitonin levels can assist with this question by enabling earlier termination of therapy.[7] Rather, we tend to select fixed durations of therapy knowing that we are overtreating some (if not most) patients because we cannot distinguish individual treatment needs, and we want to be sure that the duration we select will maximally cure everyone we treat. Our desire to maximize cures across a population has led us to expand durations of therapy over many decades based on increments of Constantine Units. Fortunately, more recent randomized controlled trials now tell us with great confidence that shorter courses of antibiotic therapy are as effective as longer courses, with the added benefit of reducing the exposure of patients to antibiotics. Reduced exposure intrinsically reduces the risk of adverse events and of selective pressure that drives resistance in our microbiomes.

Thus, shorter is indeed better. The thought is no longer new; it is maturing. It is based on real, repeated, high-quality randomized controlled trials across multiple types of infections. Medical staffs of hospitals should pass expected practices around short-course antibiotic therapy to encourage their providers to practice modern antiinfective medicine. National guidelines for specific types of infections and regulatory standards for clinical trial conduct should also be updated.[3,8] In short, it is time for the medical community to support changing our old habits and help to transform how we use and protect the rapidly eroding societal trust[8] that is effective antimicrobial therapy.

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TABLE.

Infections for which Short-Course Antibiotic Therapy Is Equivalent in Efficacy to Longer Therapy[1]

Disease	Short Course Studied (days)	Long Course Studied (days)	Result
Acute bacterial sinusitis	5	10	Equal
Acute exacerbation of chronic bronchitis and obstructive pulmonary disease	≤5	≥7	Equal
Intraabdominal infection	4	10	Equal
Osteomyelitis	42	84	Equal
Pneumonia, community-acquired	3–5	7–10	Equal
Pneumonia, nosocomial (including ventilator-associated)	≤8	10–15	Equal
Pyelonephritis	5–7	10–14	Equal
Skin infections (cellulitis, major abscesses, wound infections)	5–6	10–14	Equal