Guideline Tyranny: Primum non nocere

Stephen G. Baum and Anna Kaltsas

1Albert Einstein College of Medicine and 2Infectious Diseases Training Program, Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, New York

Toward the end of the 20th century, clinical guidelines proliferated that had the laudable aim of bringing best practices to bear on the unnecessary variability of medical care. New guidelines have continued to appear that span the entire spectrum of medical and surgical practice. Meanwhile, older guidelines have been continually updated.

Community-acquired pneumonia (CAP), one of the most common conditions to lead to hospitalization in the United States, has been increasing among adults aged >65 years [1], and CAP was the focus of one of the earliest clinical guidelines. Several national professional societies, including the Infectious Diseases Society of America and the American Thoracic Society, first published their own guidelines on CAP and later collaborated on consensus-driven guidelines [2].

In 1997, a single publication on the treatment of CAP in elderly patients provided data indicating that patients with CAP had improved survival rates if they received antimicrobial therapy \( \leq 8 \) h after first being seen in an emergency department setting [3]. This retrospective study involved 14,069 patients and demonstrated a 15% lower odds of mortality during the subsequent 30 days if antibiotics were administered within 8 h. On the basis of the results of this study, the Health Care Finance Agency (now the Centers for Medicare and Medicaid Services [CMS]), promulgated the recommendation that all patients with CAP be treated within 8 h after admission to the emergency department. In 2004, the recommended duration until treatment was reduced to \( \leq 4 \) h, in response to a CMS-sponsored study that demonstrated slightly improved mortality rates in older patients who received antibiotics within a 4-h window [4].

Critics of the CMS-sponsored study point to several inconsistencies, such as the increased mortality rate if antibiotics are given \( \leq 2 \) h after admission but decreased mortality rate if they are given at 4 h [5]. They also point out that antibiotics take several days to impact the outcome of pneumococcal pneumonia and offer alternative explanations for the study findings. One such explanation includes the possibility that altered mental status and atypical presentations of CAP—particularly common phenomena in elderly patients—can be markers of underlying co-morbidities that, in and of themselves, predict a poor prognosis. These co-morbidities and atypical presentations, rather than the delay in antibiotic administration that they often occasion, may be the causes of adverse outcomes.

In addition, patients who receive antibiotics in a timely manner at presentation to the hospital may demonstrate better outcomes not just because they received antibiotics within \( \leq 4 \) h after admission, but because health care providers—either consciously or not—were also treating signs of early sepsis, with oxygen administration and fluids, etc. It is known that early goal-directed treatment of sepsis results in better patient outcomes [6].

Nonetheless, this 4-h time span has now been adopted as a standard of care and, in many states, is one of the core measures on which the quality of care at a given hospital is assessed. The pay-for-performance initiative is under final consideration by the CMS, which has signaled that it will embrace the standard as an easily measurable quality index on which hospital reimbursement can be predicated. Rarely has such a far-reaching policy been based on so little evidence, and rarely has such a decision augured more strongly for adversely affecting the public health because of its unanticipated consequences. What are these consequences, and are they really unanticipated?

Perhaps the most ubiquitous infectious disease problem that will affect us in the next few decades is the emergence of resistance to antimicrobial agents in bacteria and other microorganisms. Although AIDS has and will decimate populations of millions of people, and although the evolution of an avian influenza virus with capacity for human-to-human transmission would be devastating, emerging drug resistance, which is very much a part of the present disease scene, has the capacity to affect every human being adversely. Resistant (and therefore lethal) pneumococcus, Staphylococcus species, Clostridium difficile, Mycobacterium tuberculosis, and...
many other organisms abound, and new examples of resistance are reported daily. We maintain that enforcement and rewarding through pay-for-performance measures of the rule that all patients who present with CAP be treated within 4 h (or even 8 h) is predicated on minimal and highly suspect evidence and has the potential to cause great harm by increasing the overuse of antibiotics, thereby raising the potential for emerging drug resistance. Several factors make this situation even worse than one might imagine at first blush. The first of these factors is that large epidemiologic studies have shown that up to 29% of patients hospitalized with CAP actually had a viral infection [7, 8]. This figure probably underestimates the real value, given that up to 60% of patients who are admitted to the hospital for CAP never have an etiologic agent identified [8, 9], and that a large proportion of cases of pneumonia among these patients would likely have an underlying viral—rather than bacterial—etiologic, as indicated on the basis of the relative difficulty in identifying viruses. Therefore, perhaps one-half of patients with CAP who receive antibiotics within 4 h after hospital admission would be treated with agents that are not efficacious.

The second factor relates to the current circumstances in which most CAP therapy is instituted in the emergency department: often without sufficient proof that the patient is experiencing pneumonia rather than upper respiratory infection. In unpublished data from quality improvement studies, up to one-half of patients admitted with a diagnosis of pneumonia only had an upper respiratory tract infection. A recent published study confirmed these data and reported a >2-fold increase in misdiagnosis (or overdiagnosis) of CAP during the period 2003–2005 [9]. In addition, up to 50% of the patients for whom initial CAP treatment fails are eventually shown, after additional evaluation, to have noninfectious etiologies, such as congestive heart failure, interstitial pulmonary fibrosis, Wegener granulomatosis, pulmonary embolism with lung infarction, or cryptogenic organizing pneumonia, among others [10]. Finally, the alarming increase in the rate of C. difficile colitis, with its attendant high morbidity and mortality, is directly traceable to antibiotic use, providing yet another reason to minimize unnecessary administration of antimicrobials.

Even if rapid antimicrobial therapy for bacterial pneumonia resulted in improved outcome of this condition, it is clear from the data reviewed here that millions of patients with nonbacterial pneumonia would be unnecessarily treated with antibiotics. At a time when the concerted efforts of infectious diseases experts are directed toward minimizing unnecessary antimicrobial treatment, the CAP guidelines are virtually guaranteed to increase this overuse. Therefore, it would appear that the practice of rapid antimicrobial therapy has every likelihood of contributing to the emergence of bacterial resistance and that this consequence can no longer be considered “unanticipated.” The accrediting and funding agencies should not use the application of these timing guidelines to measure quality of care or to pay for performance.

Acknowledgments


References