Reply to Musher et al

TO THE EDITOR—We thank Musher et al [1] for their comments about our article [2] and their thorough review of their recently published study [3] that was similar to ours. We concur that the practice of medicine remains an art that is not well served by strict adherence to treatment algorithms and overreliance on any single test result without thoughtful interpretation in the proper clinical context. However, we also believe that medicine should also be guided by valid scientific data, and there is now a large body of evidence that indicates that serum biomarkers, although not perfect, are useful for patient management [4].

We wish to reemphasize that the goal of our study was to determine the incidence of bacterial infections that complicate viral respiratory infections, a highly debated issue for which there are very few data. To this end, we used standard assays to identify bacterial infection but also included elevated procalcitonin level to provide the most conservative estimate. We were not attempting to validate the serum procalcitonin level as a marker of bacterial infection, nor did we state or imply that this test should be the starting point in algorithms to withhold antibiotics. Most experts would agree that the diagnosis of bacterial respiratory infection by use of traditional microbiologic techniques is remarkably difficult and that the acquisition of good-quality sputum specimens remains very problematic. Despite Herculean efforts to do so, we successfully obtained adequate samples within 6 hours of antibiotic administration in only 51% of subjects, whereas Musher et al collected adequate samples within 18 hours of antibiotic administration from only 31%. At present, there are no sensitive and specific diagnostic tests for bacterial respiratory infection. So how do we attempt to answer this important question? Musher et al acknowledge that an elevated serum procalcitonin level is generally consistent with a bacterial infection, so we are uncertain as to why they would have concerns that we used both traditional microbiologic data and elevated procalcitonin levels for the most inclusive definition for bacterial complications of viral infection. Most would agree that the use of specific microbiologic testing alone would have significantly underestimated the problem.

An important difference between our study and the study by Musher et al is that we did not limit inclusion to patients hospitalized with pneumonia. Since both the Infectious Diseases Society of America and the American Thoracic Society recommend early empirical antibiotic therapy for patients with pneumonia, the question of the incidence of bacterial complications and the usefulness of serum biomarkers in this group with viral infection may be less relevant. However, many patients hospitalized with respiratory virus infection do not have pneumonia; rather, they have other conditions, such as acute exacerbation of chronic obstructive pulmonary disease (COPD), acute exacerbation of asthma, acute bronchitis, and decompensated chronic medical conditions, such as congestive heart failure. The use of antibiotics for these syndromes is not clearly defined, yet it is nearly universal among hospitalized patients. In our previous study of COPD to which Musher et al refer, we found that the serum procalcitonin level was significantly higher in...
patients with COPD who had pneumonia than in those with exacerbations without pneumonia [5]. However, the procalcitonin level did not provide good discrimination between bacterial and viral nonpneumonic exacerbations. The statement that the procalcitonin level was low in 11 of 16 patients with bacterial and viral pneumonia is incorrect because these subjects had no radiographic evidence of pneumonia. Our conclusions, based on this prior study and our current study, are that serum biomarkers may not be as useful for less invasive forms of respiratory infection and that examination of sputum remains an important tool for the clinician. However, given the issues of bacterial colonization in patients with COPD, the only way to really know whether sputum findings or an elevated procalcitonin level is the best predictor of the need for antibiotics in exacerbations of COPD without pneumonia is to perform a randomized clinical trial.

We believe our study provides a relatively accurate estimate of the incidence of bacterial complications of serious respiratory viral infection, given the current limitations of diagnostic testing.

Because 60% of the patients in our study had no evidence of bacterial infection and 4 deaths due to *Clostridium difficile* infection occurred in this group, we think it is appropriate for clinicians to consider whether broad-spectrum antibiotics are needed in all patients with documented viral infection, particularly those without clear evidence of pneumonia. We stand by our concluding statement that further studies are needed to develop treatment algorithms that combine biomarkers and clinical parameters, so that antibiotics can be safely discontinued in some patients hospitalized with viral infection.

Notes

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References


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