Serum Procalcitonin Level, Viral Polymerase Chain Reaction Analysis, and Lower Respiratory Tract Infection

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To the Editor—The recent study by Falsey et al [1] and our study from earlier this year [2] share many similarities regarding the diagnosis of acute lower respiratory tract infection but have a very important difference. Falsey et al included adults who were hospitalized for a respiratory infection, whereas we required the presence of a newly recognized pulmonary infiltrate. Both studies were meticulous in their attempts to establish etiologic diagnoses. Similar to the study by Falsey et al, in our study, about 95% of all patients had blood specimens obtained for culture, urine samples obtained for detection of pneumococcal and Legionella antigens, a nasal swab specimen collected for viral polymerase chain reaction (PCR) analysis, and a serum specimen collected for procalcitonin analysis. Sputum was submitted for Gram stain and culture in 83% of cases (although in many, the specimen was inadequate or obtained >18 hours after antibiotics had been administered). Both studies identified a bacterial cause in a minority of cases (19% in their study and 23% in our study), and both specifically identified a viral and a bacterial coinfecting agent in a similar proportion of cases (64 of 842 [7.6%] in their study and 11 of 215 [5.1%] in our study).

The important difference between the 2 studies is that Falsey et al regarded the serum procalcitonin assay sufficiently reliable and, in their analysis, stratified patients on the basis of these results into those with bacterial infection and those
with nonbacterial infection. In contrast, although we agree that an elevated serum procalcitonin level is generally consistent with the presence of bacterial infection [3, 4], we did not believe that it can be used reliably to stratify individual patients with documented lower respiratory tract infection into those with bacterial infection and those with nonbacterial infection. Accordingly, in our study, we regarded the procalcitonin level as a variable that required validation. Mean procalcitonin levels were 5.57 ng/mL in patients with proven bacterial pneumonia and 1.53 ng/mL in patients with presumptive bacterial pneumonia, supporting the notion that an elevated procalcitonin level is generally consistent with bacterial infection (Figure 1). However, In 19 of 60 patients (31.7%) with bacterial infection (6 with proven infection [isolates from a normally sterile site], and 13 with presumptive infection [Gram stain and culture of sputum showing a typical lower respiratory tract pathogen]), the procalcitonin level was <0.25 ng/mL, and in 14 of 60 patients (23.3%) cases (3 with proven infection, and 11 with presumptive infection), the procalcitonin level was <0.1 ng/mL. Of patients with documented bacterial infection and a procalcitonin level of <0.25 ng/mL, 13 were in Pneumonia Patient Outcomes Research Team (PORT) risk group 4 (PORT score index [PSI], 4); 9 of these had a procalcitonin level <0.1 ng/mL. Importantly, these results show that, despite the general association of elevated procalcitonin level with bacterial infection, a low procalcitonin level in a patient hospitalized for pneumonia clearly does not exclude the possibility of serious bacterial infection. Although we only studied procalcitonin level on admission, repeating the test the following day regularly yields a similar result [5].

This finding is not new; a careful reading of earlier articles relating procalcitonin level and bacterial infection shows that the procalcitonin level is regularly low (normal), in a varying proportion of documented bacterial infections, generally 20%–30% [5–7]. In fact, Falsey et al [5] previously published a cautionary note about excess reliance on the procalcitonin level, showing that 11 of 16 patients with concomitant bacterial and viral pneumonia had normal procalcitonin levels. It is, therefore, unclear why, in their current study, they stratified patients on the basis of procalcitonin levels.

Why is all this important? Albrich et al have stated [8] and Falsey et al imply that a serum procalcitonin level can serve as an important starting point in an algorithm for treating patients who have lower respiratory tract infections. In contrast, our results clearly show that a low serum procalcitonin level cannot be used as the basis for deciding whether to treat a patient who is hospitalized for pneumonia. A further point of agreement between Falsey et al’s study and ours is that a substantial proportion of patients who have bacterial lower respiratory tract infections are coinfected with viruses. Our coinfected patients tended to have low procalcitonin levels (Figure 1). Thus, even a low procalcitonin level and a positive result of a viral PCR assay—data that might be available very soon after admission—do not justify the withholding of antibiotics in a patient hospitalized for pneumonia. Since our study was based on data from patients who were hospitalized for pneumonia, we cannot make any inference about those who are treated as outpatients or who may not have pneumonia.

Because a test that distinguishes bacterial infection from other causes of febrile disease remains elusive, we need to make better use of traditional techniques, such

![Figure 1.](https://academic.oup.com/jid/article/209/4/631/2193548)
as inducing sputum for Gram stain and culture, while developing newer ones, such as quantitative bacterial PCR analysis [9], to identify bacterial pathogens.

Our findings do provide reassurance that, for the time being, the practice of medicine continues to involve more than algorithms and that the art of medicine is not dead.

Note

Potential conflicts of interest. All authors: No reported conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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References