

## Procalcitonin-Guided Treatment of Respiratory Tract Infections

MARK EBELL, MD, MS, *University of Georgia, Athens, Georgia*

This guide is one in a series that offers evidence-based tools to assist family physicians in improving their decision making at the point of care.

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### Clinical Question

Does procalcitonin have a role in guiding treatment of respiratory tract infection?

### Evidence Summary

Procalcitonin is a precursor to calcitonin. The final step in the synthesis of calcitonin is inhibited by cytokines and endotoxin released during bacterial infections; therefore, procalcitonin levels are selectively elevated in patients with bacterial infections.<sup>1</sup> Therapy guided by procalcitonin levels has been proposed for a variety of settings, from the outpatient management of respiratory tract infections to the care of critically ill patients with sepsis. The focus of this review is the use of procalcitonin levels to guide the care of patients with acute respiratory tract infection.

Several studies have evaluated usual care of respiratory tract infection versus procalcitonin-guided therapy.<sup>2-4</sup> In one study, 243 patients presenting to the emergency department with acute respiratory tract infection (i.e., dyspnea, cough, or both) were randomized to receive antibiotic therapy or therapy guided by procalcitonin levels.<sup>2</sup> Patients with cystic fibrosis, active tuberculosis, or nosocomial pneumonia, and those severely immunocompromised were excluded. Antibiotics were strongly discouraged with procalcitonin levels less than 0.1 ng per mL, discouraged with levels 0.1 to 0.24 ng per mL, encouraged with levels 0.25 to 0.50 ng per mL, and strongly encouraged with levels greater than 0.5 ng per mL. The final diagnosis was pneumonia in 36 percent of patients, chronic obstructive pulmonary disease (COPD) exacerbation in 25 percent, acute bronchitis in 24 percent, and asthma exacerbation in 5 percent. Procalcitonin-guided therapy reduced antibiotic use from 83 to 44 percent ( $P < .0001$ ) without

changes in quality-of-life scores, laboratory or physiologic parameters, hospital admissions, length of hospitalization, or mortality.

A second study included 302 adults admitted to the emergency department for community-acquired pneumonia.<sup>3</sup> Patients were randomized to receive usual care or therapy guided by procalcitonin levels (antibiotics were strongly discouraged with procalcitonin levels less than 0.1 ng per mL, discouraged with levels 0.1 to 0.25 ng per mL, encouraged with levels greater than 0.25 ng per mL, and strongly encouraged with levels greater than 0.5 ng per mL). Patients with cystic fibrosis, active tuberculosis, or nosocomial pneumonia, and those severely immunocompromised were excluded. Patients in the procalcitonin group were less likely to receive an antibiotic on admission compared with those in the control group (85 versus 99 percent, respectively) and had a shorter median duration of antibiotic therapy (five versus 12 days, respectively); otherwise, the two groups had similar outcomes.

A third study included 226 adults hospitalized for a COPD exacerbation.<sup>4</sup> Patients were randomized to receive usual care or therapy guided by procalcitonin levels (antibiotics were not recommended with procalcitonin levels less than 0.1 ng per mL, were optional with levels 0.1 to 0.25 ng per mL, and were recommended with levels greater than 0.25 ng per mL). Patients who received procalcitonin-guided care were less likely to receive an antibiotic than those in the control group (40 versus 72 percent, respectively,  $P < .0001$ ). There was no difference between groups in days to the next exacerbation, exacerbations in the next six months, lung function, symptoms, functional status, or length of hospitalization.

Procalcitonin has also been studied for its usefulness in predicting mortality. In a study of 1,651 patients admitted with community-acquired pneumonia, procalcitonin levels were performed within a mean of 1.3 hours after admission.<sup>5</sup> Scores on the CURB-65 (Confusion, Uremia, Respiratory rate, low Blood pressure, 65 years of age or older) and Pneumonia Severity Index, which determine prognosis for pneumonia, were calculated for each patient, and procalcitonin and the two prognostic scores were correlated. With all three, the risk of 30-day mortality increased with increasing values or scores. Procalcitonin levels added little to the information about prognosis in low-risk patients (defined as patients in Pneumonia Severity Index class I, II, or III or in CURB-65 group 1). However, among high-risk patients, those with procalcitonin levels less than 0.1 ng per mL had a much better prognosis, with negative likelihood ratios between 0.09 and 0.18.

General guidelines for interpretation of procalcitonin levels are shown in *Table 1*.<sup>2-4</sup> However, there are several caveats regarding the use of procalcitonin to guide decisions about antibiotic therapy in patients with acute respiratory tract infection. Although point-of-care tests for procalcitonin levels have been developed, they require a more sophisticated laboratory than those available in most family medicine offices. The tests are also relatively costly (\$50 to \$100). Finally, the three key studies of their use in patients with acute respiratory tract infection were all performed by the same group, were funded by the company that makes the test, and included an investigator who has received substantial lecture and advisory board fees related to its use.<sup>2-4</sup>

### Applying the Evidence

A 58-year-old man presents with cough, fever, and productive sputum that have persisted for

**Table 1. Interpretation of Procalcitonin Test Results in Patients with Acute Respiratory Tract Infection**

<i>Procalcitonin level</i>	<i>Suggested action</i>
< 0.1 ng per mL	Antibiotics strongly discouraged
0.1 to 0.24 ng per mL	Antibiotics discouraged
0.25 to 0.50 ng per mL	Antibiotics encouraged
> 0.50 ng per mL	Antibiotics strongly encouraged

*Information from references 2 through 4.*

two days. He has well-controlled hypertension and is otherwise healthy. Chest radiography reveals no infiltrate. His procalcitonin test result is 0.05 ng per mL. Should you prescribe an antibiotic?

*Answer:* Because bacterial infection is unlikely, you recommend rest, cough suppressants, and follow-up in three days, but no antibiotics.

*Address correspondence to Mark Ebell, MD, MS, at ebell@uga.edu. Reprints are not available from the author.*

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