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Original Contributions

C-REACTIVE PROTEIN TESTING DOES NOT DECREASE ANTIBIOTIC USE FOR ACUTE COUGH ILLNESS WHEN COMPARED TO A CLINICAL ALGORITHM

Ralph Gonzales, MD, MSPH,* Eva M. Aagaard, MD,† Carlos A. Camargo Jr, MD, DRPH,‡ O. John Ma, MD,§ Mark Plautz, MD,‖ Judith H. Maselli, MSPH,* Charles E. McCulloch, PHD,¶ Sara K. Levin, BS,* and Joshua P. Metlay, MD, PHD#

*Department of Medicine, University of California, San Francisco, San Francisco, California, †Department of Medicine, University of Colorado and Denver and Health Sciences Center, Denver, Colorado, ‡Department of Emergency Medicine, Massachussetts General Hospital, Boston, Massachusetts, §Department of Emergency Medicine, Oregon Health and Sciences University, Portland, Oregon, ‖Veterans Affairs Medical Center, Medicine Service (111), Kansas City, Missouri, ¶Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, California, and #VA Medical Center, and the University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Reprint Address: Ralph Gonzales, MD, MSPH, Department of Medicine, University of California, San Francisco, 3333 California Street, Box 1211, San Francisco, CA 94118

□ **Abstract—Background: Antibiotics are commonly overused in adults seeking emergency department (ED) care for acute cough illness. Objective: To evaluate the effect of a point-of-care C-reactive protein (CRP) blood test on antibiotic treatment of acute cough illness in adults. Methods: A randomized controlled trial was conducted in a single urban ED in the United States. The participants were adults (age ≥ 18 years) seeking care for acute cough illness (≤ 21 days duration); 139 participants were enrolled, and 131 completed the ED visit. Between November 2005 and March 2006, study participants had attached to their medical charts a clinical algorithm with recommendations for chest X-ray study or antibiotic treatment. For CRP-tested patients, recommendations were based on the same algorithm plus the CRP level. Results: There was no difference in antibiotic use between CRP-tested and control participants (37% [95% confidence interval (CI) 29–45%] vs. 31% [95% CI 23–39%], respectively; $p = 0.46$) or chest X-ray use (52% [95% CI 43–61%] vs. 48% [95% CI 39–57%], respectively; $p = 0.67$). Among CRP-tested participants, those with normal CRP levels received antibiotics much less frequently than those with indeterminate CRP levels (20% [95% CI 7–33%] vs. 50% [95% CI 32–68%], respectively; $p = 0.01$). Conclusions: Point-of-care CRP testing does not seem to provide any additional value beyond a point-of-care clinical decision support for reducing antibiotic use in adults with acute cough illness.** © 2011 Elsevier Inc.

□ **Keywords: C-reactive protein; acute respiratory tract infections; quality improvement; antimicrobial agents**

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INTRODUCTION

Antibiotics are frequently prescribed to adults with acute cough illness (about 50–80% of visits) despite meta-analyses and practice guidelines that do not support routine antibiotic treatment (1–3). In addition, physicians are increasingly choosing broad-spectrum antibiotics over narrow-spectrum agents (4,5). Because patient and physician educational campaigns have had only a modest impact on reducing the overuse of antibiotics for acute

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respiratory tract infections (ARIs), new strategies such as decision support and diagnostic test strategies have been sought to help solve this problem (6–8). Because the small subset of patients with uncomplicated acute cough illness who are likely to benefit from antibiotics are those with community-acquired pneumonia, strategies that improve the accuracy of pneumonia diagnosis could improve targeting of antibiotics to appropriate patients.

Serum levels of acute inflammatory mediators, such as C-reactive protein (CRP) and procalcitonin, can help distinguish bacterial infections in hospitalized and ambulatory patient populations. Among outpatients with ARIs, CRP levels ≥ 10 mg/L are highly sensitive (80–90%), but modestly specific (50–70%) for diagnosing radiographic pneumonia; and point-of-care tests for CRP and procalcitonin have shown potential to reduce antibiotic use in a variety of clinical settings (9–11). However, these studies have not compared point-of-care testing with point-of-care clinical decision support. In this trial we have examined the incremental effect of point-of-care CRP testing on a clinical algorithm for assessing the probability of pneumonia in adults with acute cough illness. We hypothesized that providing clinicians with a CRP level at the point of care, along with a clinical algorithm for interpreting the results, would lead to lower antibiotic prescription and chest X-ray study ordering rates compared to physicians managing patients with the clinical algorithm alone.

METHODS

We conducted a randomized, controlled trial of the CRP testing algorithm at an emergency department (ED) that supports a 3-year emergency medicine residency program, with an annual patient volume of 58,000, that is located in a large, midwestern metropolitan city in the United States. This ED served as one of eight control sites during the previous 2 years as part of the Improving Antibiotic Use in Acute Care Treatment (IMPAACT) Trial, during which the average antibiotic prescription rate for adult patients with non-pneumonic acute cough illness ranged between 53% and 57% (8). The trial received human subjects protection committee approval from the intervention site, as well as from the institutions of the principal investigators (RG, JPM). The trial was registered at clinicaltrials.gov (NCT00221351) in advance of patient enrollment.

The trial was conducted between November 2005 and March 2006. At the beginning of the trial, ED attendings and housestaff were given a 1.5-h educational seminar that reviewed evidence-based recommendations for the evaluation and treatment of acute cough illness and community-acquired pneumonia, as well as the current evidence on CRP levels as adjuncts in the diagnosis of pneumonia (or other antibiotic-responsive illnesses) (1,10,12,13).

A study nurse approached a potential study participant immediately after triage nurse examination if the patient was seeking care for an acute illness with symptoms referable to the sinuses, throat, or chest. Inclusion criteria included age ≥ 18 years; new cough present ≤ 21 days; at least one other ARI symptom (fever, sore throat, night sweats, body aches, nasal or chest congestion, shortness of breath); and availability for a telephone follow-up interview in 2–4 weeks. Exclusion criteria included symptoms or signs requiring urgent evaluation, cystic fibrosis, immunodeficiency, and inability to provide informed consent. We tracked the total number of subjects approached and eligible for enrollment in 4 of the 5 months of the study and projected the total number of approached and eligible patients for the full 5-month period.

Randomization was performed by the data coordinating center staff using a random-number generator. Eligible subjects who provided informed consent were randomized to either a CRP test using a bedside fingerstick, whole blood specimen (QuikRead CRP, Orion Corporation, Orion Diagnostica, Espoo, Finland) performed by the study nurse, or to a control group; and the result

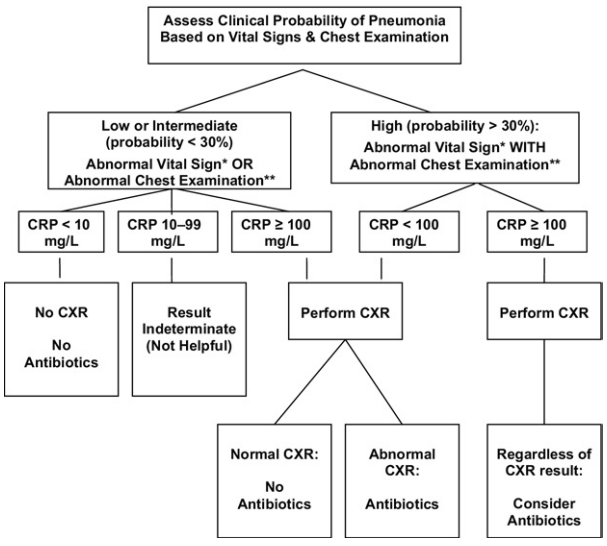

Figure 1. C-reactive protein-based algorithm for guiding chest X-ray and antibiotic treatment decisions in adults with acute cough illness. *Abnormal vital signs include one or more of the following: oral temperature ≥ 37.8°C, heart rate ≥ 100 beats/min, respiratory rate ≥ 24 breaths/min, or O_2 saturation ≤ 94%. **Abnormal chest examination such as focal decreased breath sounds, crackles or rales suggestive of consolidation. CRP = C-reactive protein; CXR = chest X-ray.