

CORRESPONDENCE



Community-Acquired Pneumonia Requiring Hospitalization

TO THE EDITOR: With regard to the results of the Centers for Disease Control and Prevention (CDC) Etiology of Pneumonia in the Community (EPIC) study reported by Jain et al. (July 30 issue),¹ two related points warrant emphasis. First, although the authors found an increased incidence of pneumonia with increasing age, this study shows that “old” is not so old. The results showed that half of all hospitalizations for community-acquired pneumonia in adults involved patients who were 57 years of age or younger.

Second, as noted by the authors, concerted efforts to define a microbial cause did not reveal a pathogen of especially great concern. Responsible microbes were not detected in nearly two thirds of the patients, and no single microbe was associated with more than a small fraction of cases (<9% for every microbe). Thus, pneumonia in adults is less about the microbe and more about the host. The combination of immunemediating antimicrobial activities with homeostatic pathways limiting physiological disruption provides an integrated host defense² that increases during childhood, in part because of adaptive immunity to respiratory infections,³ but it then becomes compromised by diverse factors during aging, with the result that the risk of

pneumonia is increased.⁴ A person’s susceptibility to pneumonia cannot be measured. New tools are needed to diagnose, track, and counter susceptibility to pneumonia, a chronic disease of aging that has not been effectively addressed.

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TO THE EDITOR: Jain et al. report that approximately two thirds of the hospitalized patients with pneumonia in their study were in a low-risk class with respect to the risk of death. The reasons why all these patients with pneumonia were hospitalized are unclear, particularly because clinical-practice guidelines¹ suggest that these patients may be safely cared for at home. Admission of patients in whom the severity of pneumonia was low resulted in a population in which a quarter of the patients had a benign type of disease caused by viruses.

These results have important implications with respect to the generalizability of the results and the actual need for antibiotic agents in an era of increased antimicrobial resistance. We strongly recommend caution in applying the results of this study, because clinicians do not

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regularly perform all these tests in patients in whom pneumonia is not severe. The fact that the EPIC cohort had such a low mortality and short hospital length of stay indicates the need for validated severity scores that go beyond microbiologic identification and provide information that is useful in the decision-making process of caring for patients with pneumonia.²

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TO THE EDITOR: Jain et al. implicate “relatively insensitive diagnostic tests” to explain why a causative pathogen was not identified in 62% of cases of community-acquired pneumonia in their study. Although this notion is supported, in part, by studies that use more invasive diagnostic tests,¹ as-yet unrecognized pathogens also may play an important role.

Using techniques that were nearly identical to those used by Jain et al., we were unable to identify an etiologic agent in 51% of cases of community-acquired pneumonia.² In 29 of these cases, microscopic examination of a freshly obtained sputum specimen that contained more than 10 white cells per epithelial cell³ showed that 16 specimens had moderate-to-large numbers of bacteria and 13 had few or no bacteria. These findings suggest that still-unidentified bacteria in normal oral flora and nonbacterial pathogens may cause pneumonia in adults. This is not surprising; only a few decades ago, nontypable *Haemophilus influenzae*⁴ and *Moraxella catarrhalis*⁵ were not regarded as causes of pneumonia. Perhaps the era of next-generation sequencing will result in the discovery of new pathogens.

Alternatively, some cases without an identifiable pathogen might be explained by noninfectious causes; our study² showed a noninfectious cause in 17% of patients who were admitted because of community-acquired pneumonia.

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TO THE EDITOR: Results of the study by Jain and colleagues that showed a pathogen-detection rate of only 38% are striking. We think that the comments made regarding radiologic evaluation are debatable. It is true that confirmation of pneumonia “by a board-certified chest radiologist” increases the reliability of the diagnosis; however, observer variability among radiologists is not low, and their findings may not always correlate with the final clinical assessment. Although radiographic confirmation increases the specificity of the case definition, it may not always be as high as is anticipated.

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THE AUTHORS REPLY: As noted by Mizgerd, host factors, including the patient's age, underlying conditions, and immunologic factors resulting from previous exposures and vaccination, play a major role in community-acquired pneumonia.¹ These factors are important areas for future study.

Patients in the EPIC study were hospitalized on the basis of decisions by the treating clinicians, and study personnel had no role in those decisions. Marcos et al. are correct that 70% of enrolled adults in our study had a CURB-65 score of 1 or less (the CURB-65 score, which ranges from 0 to 5, is calculated by assigning 1 point each for new-onset confusion, uremia [blood urea nitrogen >19 mg per deciliter], a high respiratory rate [≥ 30 breaths per minute], a low systolic [< 90 mm Hg] or diastolic [≤ 60 mm Hg] blood pressure, and an age of ≥ 65 years, with a higher score indicating a higher risk of death within 30 days), and 65% had a Pneumonia Severity Index (PSI) risk class of 3 or less (on a scale of 1 to 5, with higher classes indicating a greater risk of death; class 1 to 3 indicates a low risk of death, class 4 moderate risk, and class 5 high risk). Together, these ratings indicate a low risk of death at 30 days. However, despite advocacy for the use of these scoring systems for admission decisions, they are not universally applied in clinical practice. Other factors, including underlying conditions, the need for supplemental oxygen, the ability to receive oral antimicrobial agents, the ability of the patient and his or her family to cope with the illness, and concurrent acute medical conditions, often affect admission decisions.² Although approximately 30 to 35% of adults with community-acquired pneumonia in the United States are in a higher-risk PSI class (class 4 or 5), an estimated 72% of adults who are evaluated in emergency departments for pneumonia are hospitalized; this highlights the large number of patients with lower severity scores who are hospitalized.³ It is also important to note that independent of the severity score, 99% of the adults who were enrolled in our study received antibiotics on an inpatient basis, but bacteria were detected more frequently among patients in the intensive care unit, patients who had a PSI class of 4 or 5, or both.

The comments by Musher and Abers are important in that they highlight the need for improved diagnostic tests to identify known pneumonia pathogens and expand the search for microbes that are not yet identified as being

pneumonia pathogens. Comprehensive sequencing approaches and other innovative methods for the discovery of pathogens might contribute to expanded knowledge and improve treatment algorithms at the point of care. We also agree that noninfectious causes could have contributed to illnesses that met the case definition of pneumonia in the EPIC study, since there is overlap between the clinical and radiographic presentation of pneumonia and that of chronic cardiopulmonary diseases.

Finally, as Kaya et al. emphasize, radiologic evaluations can be subjective regardless of the level of experience and clinical training of the radiologist.⁴ Our study sought to increase specificity with the use of a common standard of radiographic confirmation in the case definition and study protocol and a single board-certified chest radiologist in each of the two cities where the study was conducted. Review of a 10% random sample of radiographs from adults in our study showed that the interrater percent agreement between the two study radiologists was 86% (95% confidence interval, 81 to 89). The diagnosis and treatment of community-acquired pneumonia remain challenging, and more accurate radiographic and microbiologic diagnostic methods are needed.⁵

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Since publication of their article, the authors report no further potential conflict of interest.

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