We agree with Drs Robberts and Schermer that the important “million-dollar question” is how to confidently detect the susceptible smokers who will subsequently develop clinically important COPD if they continue smoking. As shown by results from the Lung Health Study in middle-aged smokers with FEV1/FVC < 0.70 (see Figure 2 in our counterpoint editorial), those with an FEV1 > 70%, a threshold close to the lower limit of normal for FEV1, had a mean subsequent loss of FEV1 near normal (~1.2% per year). Only below the middle of GOLD stage 2 was the mean annual loss of FEV1 relatively rapid. However, there was very wide variation, so the predictive power was very low even when all baseline characteristics of the smokers were considered in a multivariate model ($R^2 = 0.10$). Other cohort studies have collected longitudinal data from large numbers of smoking adults, including those > 65 years of age, and we encourage them to similarly analyze these data. We eagerly await new genetic and biochemical markers, which will begin to clear the smoke in our prophetic crystal ball. It is actually more like a $5 billion (or Euro) bioethical crystal ball. We agree with Drs Robberts and Schermer that the important million-dollar question is how to confidently detect the susceptible smokers who is developing COPD and had a drug to substantially dampen the progression of COPD in these susceptible smokers. Don’t hold your breath.

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Financial/nonfinancial disclosures: The authors have reported to CHEST the following conflicts of interest: Dr Enright has been paid in the past year by the American Thoracic Society, the COPD Foundation, and CME companies to prepare CME media on the topic of spirometry for COPD case finding by primary care providers. He was also paid by InterMune and Gilead to review and report the quality of pulmonary function tests for clinical trials of patients with idiopathic pulmonary fibrosis. He was trained in developing persuasive presentations and effective public speaking as a member of the Boehringer Ingelheim speakers’ bureau of key opinion leaders. He has received six-ﬁgure consulting fees from Schering and from Pfizer Inc for reviewing the quality of spirometry tests done for a study of mometasone for COPD and varenicline for smoking cessation in patients with COPD. During the past 3 years, he has been invited to give talks at the international meetings of professional organizations in which he presented evidence against the continued use of the faulty ﬁxation for the detection of COPD. In exchange for these talks, his registration fees were waived and sometimes his travel costs were reimbursed. During the past month, he was invited to do this again during the CHEST meeting in Honolulu. Dr Brusasco reported that he received funds from Lofarma for consultancies in 2008, speaking fees at conferences sponsored by Boehringer Ingelheim in 2008, fees from GlaxoSmithKline for speaking at a conference in 2010, fees from Boehringer Ingelheim for consultancy in 2009 and 2010, fees from Deep Breeze for consultancy in 2009 and 2010, fees from Dongpharma for consultancy in 2009 and 2010, fees in 2009 from GlaxoSmithKline for participating in advisory boards, fees in 2010 from Nueveden for consultation, fees from Menarini for consultancy in 2008, and fees from Novartis for participating in an Advisory Board in 2010. Dr Brusasco’s institution participated in several multicenter clinical trials ﬁnanced by pharmaceutical companies (Chiesi; Merck, Sharp & Dohme; Boehringer Ingelheim; GlaxoSmithKline; Novartis).

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References


Community-Acquired Pneumonia

Diagnostic vs Prognostic Significance of the Platelet Count

To the Editor:

We read with interest the recent report in CHEST by Mirsaiedi et al1 (February 2010) and later discussion by Georges et al2 (November 2010) regarding the prognostic significance of platelet counts in patients with severe community-acquired pneumonia (CAP) requiring hospitalization and ICU admission. However, we are not at all convinced that the platelet count alone is a prognostic indicator in adults hospitalized with severe CAP. In both pieces, information was lacking regarding the pathogen distribution, a key determinant of the platelet count.3 Because thrombocytopenia is not an acute-phase reactant, it cannot be said that thrombocytopenia with severe CAP is an indicator of severity and, thereby, is indirectly related to prognosis.3 Any CAP pathogen may present as severe CAP, depending on the cardiopulmonary and immune status of the host. Severity of CAP is largely related to these factors rather than to pathogen virulence per se. Other things being equal, Streptococcus pneumoniae is more virulent than Moraxella catarrhalis. M catarrhalis may present as severe CAP requiring hospitalization and ventilator support in a patient with borderline cardiopulmonary function. Similarly, the nonsevere bacteremic S pneumoniae form of CAP is common in patients with good cardiopulmonary function and intact humoral immunity.4 Unfortunately, specific microbiologic and host-factor data were not included in either report.2,5

However, thrombocytopenia or thrombocytosis may be associated with various CAP pathogens and may have more diagnostic than prognostic significance in adults with severe CAP. CAP pathogens that may be accompanied by thrombocytosis include Q fever and Mycoplasma pneumoniae. CAP pathogens that may be associated with thrombocytopenia include cytomegalovirus, human parainfluenza virus type 3, 2009 influenza A(H1N1),

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We read with interest the recent report in CHEST by Mirsaiedi et al (February 2010) and later discussion by Georges et al (November 2010) regarding the prognostic significance of platelet counts in patients with severe community-acquired pneumonia (CAP) requiring hospitalization and ICU admission. However, we are not at all convinced that the platelet count alone is a prognostic indicator in adults hospitalized with severe CAP. In both pieces, information was lacking regarding the pathogen distribution, a key determinant of the platelet count. Because thrombocytopenia is not an acute-phase reactant, it cannot be said that thrombocytopenia with severe CAP is an indicator of severity and, thereby, is indirectly related to prognosis. Any CAP pathogen may present as severe CAP, depending on the cardiopulmonary and immune status of the host. Severity of CAP is largely related to these factors rather than to pathogen virulence per se. Other things being equal, Streptococcus pneumoniae is more virulent than Moraxella catarrhalis. M catarrhalis may present as severe CAP requiring hospitalization and ventilator support in a patient with borderline cardiopulmonary function. Similarly, the nonsevere bacteremic S pneumoniae form of CAP is common in patients with good cardiopulmonary function and intact humoral immunity. Unfortunately, specific microbiologic and host-factor data were not included in either report.

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| Table 1—Thrombocytopenia or Thrombocytosis in Adults Hospitalized With Severe Community-Acquired Pneumonia |
|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|
| Thrombocytopenia                                 | Normal Platelet Counts                          | Thrombocytosis                                  |
| Human influenza A                                | Streptococcus pneumoniaiae^                       | Mycoplasma pneumoniaiae^                        |
| 2009 influenza A(H1N1)                          | Haemophilus influenzae                           | Q fever^                                       |
| Influenza A(H5N1)                               | Moraxella catarrhalis                            |                                                |
| Severe ARDS                                     | Legionnaires disease^                            |                                                |
| Hantavirus pulmonary syndrome                    | Chlamydia pneumoniaiae^                          |                                                |
| Cytomegalovirus                                 | Francisella tularensis^                          |                                                |
| Human parainfluenza virus-3                     |                                                |                                                |
| Respiratory syncytial virus                     |                                                |                                                |
| Psittacosis^                                    |                                                |                                                |

^Excluding hemolytic uremic syndrome or hyposplenemia/asplenia.

^Platelet count usually normal.

^Excluding cases with thrombotic thrombocytopenic purpura or hemolytic uremic syndrome.

influenza A(H5N1), severe ARDS, Hantavirus pulmonary syndrome, and so forth. Thrombocytopenia is rarely associated with bacterial CAPs but may occur rarely with psittacosis CAP^3 (Table 1). If thrombocytopenia is present with bacterial CAP, clinicians should look for an alternate explanation (eg, drug induced), or it may represent a complication (eg, hemolytic uremic syndrome). In normal hosts, most CAP pathogens are not associated with either thrombocytopenia or thrombocytosis. Normal platelet counts are the rule among typical CAP pathogens, such as S pneumoniae, Haemophilus influenzae, and M catarrhalis, as well as among atypical CAP pathogens, such as Legionella species, Chlamydia pneumoniae, and Francisella tularensis.5

In the absence of details on cardiopulmonary and humoral immune function as well as specific pathogen data, the platelet count is necessarily an imprecise prognostic indicator.5 In immunocompetent adults, it would seem that thrombocytopenia and thrombocytosis, rather than having prognostic significance, may be more important diagnostically in suggesting a specific CAP pathogen.

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REFERENCES


Response

To the Editor:

We thank Drs Cunha and Hage for their interest in our recent letter published in CHEST (November 2010).1 We reported that thrombocytopenia was an important predictor of outcome in patients with severe community-acquired pneumonia (CAP). Cunha and Hage suggest that because platelets are not an acute-phase reactant, they have no prognostic significance in patients with sepsis. Moreover, they assume platelet count to be essentially a diagnostic tool, suggestive of mostly nonbacterial pneumonia diagnosis. However, we disagree with these two suggestions.

Incidence of thrombocytopenia (platelet count < 150 x 10^9/L) in critically ill medical patients nears 40%.2 Main factors contributing to thrombocytopenia in patients with sepsis are impaired platelet production, increased consumption or destruction, or spleen platelets sequestration. Platelet consumption probably plays an important role in patients with sepsis. Thrombin is the most potent activator of platelets in vivo, and intravascular thrombin generation is a ubiquitous event in sepsis, with or without evidence of overt disseminated intravascular coagulation. Disseminated intravascular platelet activation may occur, which will contribute to microvascular failure and, thereby, play a role in the development of organ dysfunction. In the recent Infectious Diseases Society of America guidelines on the management of CAP in adults, a platelet count < 100 x 10^9/μL was a criterion for severe CAP.3 More generally, severity of thrombocytopenia has been included in different scores that evaluate critically ill patients, such as the Sequential-Related Organ Failure Assessment (SOFA) score.4 In a previous study, we reported the prevalence and prognostic value of thrombocytopenia in 822 patients admitted to the ICU.5 Causative pathogens were isolated in 490 (59.6%) patients. We assessed the relation between bacterial documentation and platelet count in 365 patients with a single isolated causative

Correspondence