Response

To the Editor:

I thank Dr. Sprung and the Corticosteroid Therapy of Septic Shock (CORTICUS) investigators for their comments on my recent article in CHEST (January 2009).1 I think we can agree that the use of corticosteroids in the critically ill is a complex and controversial topic fueled largely by the lack of high-quality scientific evidence.1 The determination of which patients are most likely to benefit from therapy with corticosteroids, as well as of the optimal dose and therapeutic strategy, awaits further investigation. This, however, does not mean that the clinician should abandon the use of these potentially life-saving drugs. In addition, as is evident from the lead article in an issue of the Wall Street Journal from 2002,2 other factors not related to scientific enquiry are at play, which further cloud the murky waters.

Clinicians need to critically appraise clinical trials (especially those published in high-profile journals), and recognize their limitations and applicability, before their “conclusions” are universally adopted. The now infamous “Intensive Insulin Therapy Trial” is a case in point.2 I believe that the CORTICUS study has a number of “limitations,” which bear on the findings of the study. Most notably, the lack of clinical equipoise led to selection bias in which patients least likely to benefit from corticosteroids were randomized to participate in the study. Using published data, I calculated that only 4% of eligible patients were enrolled into the CORTICUS trial. Furthermore, the “early” termination of therapy with corticosteroids may have led to the higher incidence of shock in the treatment group. This is supported by an apparent rebound of interleukin-6 levels in this group of patients. This suggests that a longer course of corticosteroids as well as a slower taper may be required.

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Discordance in Spirometric Interpretations Using Different Reference Equations

To The Editor:

Collen et al (November 2008)1 unveiled significant discordance in the classification of spirometric patterns of non-Hispanic white patients under the American Thoracic Society/European Respiratory Society 2005 guidelines2 when different reference equations were gauged against those of the National Health and Nutrition Examination Study III. As the American Thoracic Society/European Respiratory Society 2005 guidelines are increasingly adopted worldwide, it would be of relevance to explore whether there is similar discordance in other populations.

In Hong Kong, machine built-in equations by Knudson et al,3 old equations for the Chinese in Hong Kong by Lam et al,4 and equations for the Chinese in Singapore by Chin et al5 have been in regular use by many lung function laboratories. In 2006, Ip et al6 updated the spirometric reference equations based on local Chinese subjects who were 18 to 80 years of age. Using methods of analysis that were similar to those of Collen et al,1 we retrospectively analyzed spirometric data from 563 patients (mean age, 65 years; 63% men) who had been referred by the pulmonologists in a local tertiary cardiopulmonary center. These lung function tests were performed from May 2006 through March 2008. Discordance in classification was common when the results from equations by Knudson et al,1 Lam et al,4 and Chin et al5 were compared with those of Ip et al6 (31.4%, 27.0%, and 19.2%, respectively; all p < 0.05). Reclassification from obstructive to normal is the most common type of discrepancy. Sixty-three patients (11.2%), 56 patients (9.9%), and 67 patients (11.8%) had their results reclassified from obstructive to normal and from normal to obstructive, respectively.

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(11.9%), respectively, would be reclassified to normal from obstructive if the three sets of equations alluded were switched to those of Ip et al. It would therefore appear that such discordance could be widespread with changes in reference equations in different populations. Further research is indicated to address this outstanding question in lung function test interpretation so as to minimize the potential impact on patient care.

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Response
To the Editor:

We commend Leung and colleagues on their interest and contribution to the research on this subject. As mentioned in our article (November 2008),1 the American Thoracic Society/European Respiratory Society published guidelines2 in 2005 recommending the use of the reference values from the National Health and Nutrition Examination Study III population data set in the United States for patients 8 to 80 years of age. Currently, no guidance exists regarding the optimal reference equations for use outside the United States. The American Thoracic Society/European Respiratory Society guidelines2 only recommend that pulmonary function testing laboratories should use a reference equation “derived from a population similar to the individual subject using the same kind of instrument and testing procedure.”

The results presented by Leung et al show the greatest discordance between the reference values of Ip et al3 and Knudson et al,4 which is not surprising given the populations from which they were derived. These results reinforce the need for the development and use of reference equations that are reflective of the population being evaluated throughout the world. These equations could even be applied to specific populations in the United States. Doing so will enable clinicians here and abroad to more accurately identify and quantify pulmonary dysfunction, which may in turn result in the earlier detection and treatment of lung disease, and the conservation of valuable resources. We look forward to further research and subsequent guidance regarding these important questions.

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Miller-Fisher Variant of Guillain-Barré Syndrome
To the Editor:

I read with interest the recent article in CHEST (October 2008) by Pujar and Spinello.1 The authors concluded that glove and stocking paresthesias are key points in the Miller-Fisher variant of Guillain-Barré syndrome. I disagree. Apart from the clinical triad (ataxia, areflexia, and ophthalmoplegia), the common