received mechanical ventilation for longer than 48 h. Furthermore, the risk of epidural hematoma is a cause of concern, particularly in cardiac surgery patients, who frequently require anticoagulation. 

Finally, to our knowledge, no guidelines for the prevention of VAP have recommended TEA as a way to prevent VAP. For all of these reasons, TEA is not part of the standard of care in our cardiac surgery population.

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DOI: 10.1378/chest.09-0770

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As authors of the Corticosteroid Therapy of Septic Shock (CORTICUS) study, we readily acknowledge its limitations, especially underpowering. However, as the largest study in this field, the results cannot be simply dismissed because of their direction. Despite many patients being ineligible for the study due to concomitant steroid treatment, the research team retained clinical equipoise during patient enrollment. Although our cohort was not as severely ill as the population of Annane et al. they were more representative of the “typical” septic shock patient and significantly sicker than those Dr. Marik has suggested should receive steroids. Indeed, he suggested giving hydrocortisone with norepinephrine doses of > 0.05 to 0.1 μg/kg/min, while in the CORTICUS study the mean dose at randomization for norepinephrine was 0.4 μg/kg/min.

An increased death rate was found in patients receiving etomidate in the CORTICUS study but etomidate was not identified as an independent risk factor for death. Notwithstanding more superinfections (including new septic shock) occurring in the hydrocortisone group, repeat shock episodes were similar to the placebo group. Although reducing the dose or ceasing hydrocortisone therapy led to an increase of interleukin-6 levels on day 12, interleukin-6 levels were similar to those of the control group on day 12. Thus, these data alone are insufficient to support the prolonged application of steroids.

We have witnessed many negative outcome studies of immuno-modulatory agents in cases of sepsis. An important reason for this lack of success may be the enrollment of heterogeneous populations of patients with syndromes rather than specific diseases. While it would be convenient to have a unifying theory regarding the roles of systemic inflammation and immune dysregulation in patients with various sepsis syndromes, it is perhaps oversimplistic to believe that one therapy will be effective for all. Marik also implies that steroids should be used in patients receiving etomidate, with severe community-acquired pneumonia, during ventilatory weaning, undergoing cardiac surgery, and in critically ill patients with liver disease.

Two recent consensus statements developed by many expert panels (including the one Dr. Marik chaired) provided evidence-based guidelines for the use of corticosteroids in septic patients. Dr. Marik’s opinions diverge from these guidelines, which are more conservative in nature regarding concerns surrounding harm. Thus, specific recommendations such as starting steroid therapy based on vasopressor dose and time from presentation, tapering, and longer duration of treatment (16 to 19 days) cannot be endorsed from current data. Steroid use in septic patients without shock is counter to one of the consensus guidelines. Dr. Marik acknowledged the need for careful infection surveillance to limit the complications of corticosteroid treatment, yet, arguably, the avoidance of drug treatment (or a more limited duration of treatment) would prove far more effective in nonproven indications. It is important to provide a balanced perspective to the debate and primum non nocere.

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Steroids in Patients With Septic Shock

To the Editor:

We are concerned that Dr. Marik’s recommendations in a recent CHEST article (January 2009) on managing critical illness-related corticosteroid insufficiency contain inaccuracies, diverge from recent expert consensus statements, and may potentially compromise patient outcomes.

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DOI: 10.1378/chest.09-0329

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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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DOI: 10.1378/chest.09-0772

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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 guidelines 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 Tam 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,3 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 (12.0%) were reclassified.