against flora present in the colonized airways, suggesting that risk factors vary depending of the exposure to risk (ie, length of ventilation).

Our opinion on antimicrobial prophylaxis for VAP has been clearly stated in a recent editorial, and a randomized clinical trial to assess the effect of single-dose antibiotic administration as prophylaxis for VAP is highly recommended. Unfortunately, such evidence is lacking. Dr. Schultz suggests not using antimicrobial prophylaxis for percutaneous tracheotomies. However, as indicated before, prophylaxis for surgical neck procedures in intubated patients with colonized tracheal mucosa has a level 1 evidence. Until such studies are available, the extremely high incidence of VAP in the first days after the procedure, the distribution of pathogens, and the low predictive value of tracheal aspirates prior to tracheostomy suggest that prescription of a single dose of an antipseudomonal agent prior to the percutaneous tracheotomy is the most pertinent policy.

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REFERENCES

3 Rello J, Diaz E. Pneumonia in the ICU. Crit Care Med 2003; 31:2544–2551

Surgical Stress in ARDS Open-Lung Biopsy

To the Editor:

We read with great interest the recent case series by Patel and colleagues (January 2004). In their discussion about complica-

tions after open-lung biopsy in patients with ARDS, however, they did not refer to the contribution of surgical stress to ARDS. Major surgery, including cardiovascular surgery with cramping of the aorta and resulting in ischemia/reperfusion of the lower body, sometimes causes a systemic inflammatory response leading to the development of fatal organ-system dysfunction such as ARDS. Tumor necrosis factor or other cytokines and chemokines play important roles in systemic inflammatory response syndrome. Enhanced release of proinflammatory cytokines and chemokines results in a trigger for the production of numerous other inflammatory mediators such as nitric oxide, adhesion molecules, and eicosanoids. Rajimakers et al demonstrated the strong correlation between an increase in circulating interleukin-8 and pulmonary microvascular permeability related to aortic surgery. Indeed, we previously confirmed the pivotal roles of proinflammatory cytokines in murine acute lung injury induced by bacterial endotoxin, a similar condition for ARDS in humans. In particular, proinflammatory cytokines such as macrophage inflammatory protein-1, macrophage chemoattractant protein-1, and keratinocyte chemoattractant in the lung paralleled the magnitude of lung injury and neutrophilic inflammation in our experiments. Therefore, surgery itself may aggravate ARDS. As Patel and colleagues concluded, clinicians should give careful consideration to the selection of patients with ARDS.

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To the Editor:

We appreciate the interest of Inoue et al in our recent article (January 2004). Although we acknowledge the role of cytokines in the pathogenesis of ARDS, we would question the relevance of some of the citations in their letter. Specifically, we fail to see how acute cross-clamping causing “ischemia/reperfusion of the lower body” and/or the inhalational exposure to diesel exhaust particles have relevance to the performance of open lung biopsy in ARDS patients, because our patients’ lung injuries did not have these etiologies. However, we do acknowledge that an inflammatory response to thoracic surgery could be one mechanism underlying the deterioration in gas exchange that we occasionally observed in our ARDS patients. Of note, some data suggest that limited surgery using a thoracoscopic approach can attenuate the cytokine response compared with that with open thoracotomy. However, thoracoscopy generally requires single-lung ventilation and therefore is not usually feasible in ARDS patients. We would also caution against the use of cytokines as an end point per se without corroborative physiologic and/or clinical outcome data.

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REFERENCES

Monitoring the Adjustment of Antiasthma Medications With Adenosine Monophosphate Bronchoprovocation

To the Editor:

Airway inflammation is the major feature of asthma, and represents the major target of the pharmacologic treatment. Currently, individual adjustment of antiasthma medications is mainly based on measurements of symptoms and airflow limitations, but this approach may not be adequate and more specific surrogate markers of airway inflammation should be considered in the routine management of asthma.

The available evidence indicates that adenosine monophosphate (AMP) bronchial provocation seems to offer substantial advantages over other noninvasive markers of airway inflammation because of its exquisite sensitivity in probing changes to airway responsiveness in response to topical glucocorticosteroids, or to the effects of specific immunotherapy.

In view of this, the article by Prieto et al (October 2003), assessing the utility of the determination of airway responsiveness to inhaled AMP as a predictor for safe dose reduction of inhaled glucocorticosteroids in patients with asthma, is of great value. However, although this work appears to provide enough information to support an important role for AMP provocation in the clinical setting, a number of assertions require judicious scrutiny.

Critical to the whole study is the choice of the cut-off points for AMP sensitivity used for the statistical analysis (400 mg/mL at baseline, and a single doubling concentration decrease in the provocative concentration of AMP causing a 20% fall in FEV1 [PC20] from its baseline value 2 weeks after halving the dose of glucocorticosteroids). This is of particular value in view of the finding that a high level of sensitivity to inhaled AMP was measured in most of the patients who went on to have asthma exacerbations. By arbitrarily setting the cut-off values for PC20 too high, there is the chance of including patients with very mild asthma who are unlikely to have exacerbations. Unfortunately, an optimal cut-off value for PC20 to separate mild from severe asthma has not been established since there are no population-based data, but it would be of interest to repeat the statistical analyses utilizing a different cut-off point (eg, 100 mg/mL).

In addition, a single doubling concentration decrease in PC20 2 weeks after halving the dose of glucocorticosteroids was arbitrarily selected as an end point for establishing the predictive value of AMP responsiveness for failure in glucocorticosteroid reduction. Yet again, given that PC20 is known to return to near-baseline levels on glucocorticosteroid treatment discontinuation, it is important to consider that by arbitrarily setting a single doubling concentration decrease in PC20 2 weeks after halving the dose of glucocorticosteroids as a cut-off values, there would be less chance of identifying those patients who are likely to acquire asthma exacerbations. Perhaps repeating the statistics utilizing an alternative cut-off point (eg, three doubling concentrations decrease in PC20) would provide different results. This approach could also provide some explanation to the wide variation in individual clinical responses to glucocorticosteroid dose reduction (as suggested by the broad range in 95% confidence interval) observed in this study.

Finally, as the airway response to a direct bronchoconstrictor agonist is less sensitive to topical glucocorticosteroids, it could have been of critical importance to include methacholine provocation in the protocol so as to compare its responses to AMP in relation to the rate of asthma exacerbations provoked by glucocorticosteroid dose reduction.

Despite the emerging view that airway responsiveness to inhaled AMP may have useful clinical applications, specific recommendations for adenosine challenge testing will require further work. It is important that well-planned and well-conducted large clinical trials must be performed to demonstrate that information gained from this test will lead to improved patient management.

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