As a person dealing in complementary medicine for over a decade, I am as disappointed with negative results as you are. However, those results cannot be wiped out because of the technicalities you mention (and which we disagree with, as mentioned above).

As Sun Tzu says in the Art of War⁵: “Fight, but know where there are sufficiencies and deficiencies.” Our study does give an answer to the limited question of the effect of short-term treatment on moderate persistent asthma.

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IV Magnesium in the Treatment of Acute Severe Asthma?

To the Editor:

We read with interest the article by Silverman et al that was recently published in CHEST (August 2002)¹ regarding the administration of magnesium sulfate to adult patients with acute severe asthma. This well-done multicenter study demonstrated that the administration of 2 g IV magnesium sulfate only improves pulmonary function when administered as an adjunct to standard therapy (ie, nebulized β-agonists and IV corticosteroids) in a very select subgroup of patients (ie, those with FEV₁ ≤ 20% of predicted). On the contrary, the study found that magnesium did not decrease the hospitalization rate. However, Noppen,² in an editorial comment appearing in the same issue of CHEST as the study, asserted that “IV magnesium therapy certainly should be added to conventional treatment.”² p 397

We disagree with that statement. In our opinion, the study by Silverman et al has a critical limitation: the standard therapy used. Thus, in the last decade it has been demonstrated that the administration of anticholinergic agents to acute asthma patients who have been treated with β-agonists improves pulmonary function and reduces the hospitalization rate. The use of multiple

Table 1—Comparisons of FEV₁ Values*

<table>
<thead>
<tr>
<th>Initial FEV₁</th>
<th>Baseline</th>
<th>End of Protocol</th>
<th>MD at End (95% CI)</th>
<th>MD, Rodrigo and Rodrigo⁷/⁸</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>MD, Silverman et al¹⁰</td>
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</table>

<table>
<thead>
<tr>
<th></th>
<th>Placebo (n = 126)</th>
<th>Mg (n = 122)</th>
<th>Placebo (n = 70)</th>
<th>IB (n = 60)</th>
<th>Placebo (n = 48)</th>
<th>Mg (n = 52)</th>
<th>Placebo (n = 18)</th>
<th>IB (n = 22)</th>
<th>Placebo (n = 32)</th>
<th>Mg (n = 33)</th>
<th>Placebo (n = 38)</th>
<th>Mg (n = 25)</th>
<th>Placebo (n = 20)</th>
<th>IB (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30% predicted</td>
<td>22.7 (5.7)</td>
<td>23.1 (4.9)</td>
<td>21.7 (5.2)</td>
<td>21.3 (5.8)</td>
<td>28.1 (3.6)</td>
<td>27.3 (2.2)</td>
<td>27.1 (2.1)</td>
<td>27.4 (1.9)</td>
<td>22.0 (1.2)</td>
<td>21.9 (1.6)</td>
<td>15.9 (2.5)</td>
<td>16.3 (2.4)</td>
<td>15.0 (3.3)</td>
<td>15.5 (3.9)</td>
</tr>
<tr>
<td>≥ 30% predicted</td>
<td>26.3 (4.2)</td>
<td>27.9 (5.1)</td>
<td>25.9 (4.9)</td>
<td>25.8 (5.8)</td>
<td>30.1 (3.6)</td>
<td>29.3 (2.2)</td>
<td>29.3 (2.1)</td>
<td>29.1 (1.9)</td>
<td>25.0 (1.2)</td>
<td>25.2 (1.6)</td>
<td>20.4 (2.5)</td>
<td>21.6 (2.4)</td>
<td>19.3 (3.3)</td>
<td>19.6 (3.9)</td>
</tr>
</tbody>
</table>

*Values given as mean (SD). MD = mean difference (treatment group – placebo group); CI = confidence interval.
doses of ipratropium bromide (IB) seems indicated in the emergency department treatment of children and adults who have acute severe asthma. Studies have reported a substantial reduction in hospital admissions and significant differences in lung function favoring the combined treatment. Recently, this evidence has been included in the management guidelines of asthma exacerbation. Silverman et al recognized that the magnitude of the response to magnesium would differ if additional interventions (e.g., nebulized IB) were used, and claim for studies that consider this type of protocol.

A few years ago, we studied the effects of high and cumulative doses of salbutamol and IB in the treatment of patients with acute severe asthma (ie, FEV₁ <50% of predicted; n = 180). In a double-blind, randomized, controlled trial, we compared a regimen of salbutamol alone to salbutamol combined with IB (both drugs were administered through a metered-dose inhaler and spacer at rate of 4 puffs every 10 min). One hundred thirty patients (72% of total sample) had an FEV₁ ≤ 30% of predicted. After 3 h of treatment, subjects who had received IB had an overall 20.5% greater improvement in peak expiratory flow and a 48.1% greater improvement in FEV₁ compared with control subjects. The patients who were the most likely to benefit from the combined treatment were those with more severe obstruction (ie, FEV₁ ≤ 30% of predicted). At the end of the protocol (3 h), there was a statistical reduction in the hospital admission rate. In Table 1, we compared the FEV₁ values from our study (only patients with FEV₁ ≤ 30% of predicted) with those of the Silverman et al arrival (0 min) and at the end of the protocol (our study, 180 min; Silverman et al, 240 min). The data showed the following: (1) similar baseline values in the two studies; (2) patients in our study who had received salbutamol and IB had significant FEV₁ improvements at the end of the protocol in the three subgroups of patients, and, on the contrary, only patients with the lowest initial FEV₁ (ie, <20% of predicted) who had been treated with magnesium presented a significant improvement in pulmonary function; and (3) the ratio between the mean final differences of both studies favors our study in all subgroups studied.

In summary, the study by Silverman et al suggested that in patients with very severe acute asthma, IV magnesium administration improves pulmonary function, but it does not prove that IV magnesium should be added to the conventional treatment. We agree with Silverman et al that future studies should consider adding magnesium to a well-demonstrated protocol such as high doses of inhaled β-agonists plus IB. Finally, we give tribute to two Uruguayan physicians, Rosello and Pla, who first reported that magnesium presented a significant improvement in pulmonary function; and proven useful in these very severe cases. I therefore see no reason not to use IV magnesium sulfate in these circumstances.

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To the Editor:

I thank Drs. Rodrigo and Rodrigo for their comment on the article by Silverman et al, and on my accompanying editorial. I acknowledge their suggestion that anticholinergics might or should have been added to standard therapy in the study by Silverman et al; however, my editorial suggestion that IV magnesium sulfate should be added to standard therapy in the severest cases of acute severe asthma was not solely based on the article by Silverman et al, but mainly on two recently published meta-analyses, stating that “… magnesium sulfate appears to be safe and beneficial for patients who present with severe acute asthma. Practice guidelines need to be changed to reflect these results.” The study by Silverman et al, in my view, corroborates these suggestions.

In fact, when confronted with a patient with very severe acute asthma, with pending respiratory insufficiency and mechanical ventilation, every physician in the world will try anything at hand to avoid this. Magnesium sulfate is widely available, safe, cheap, and proven useful in these very severe cases. Therefore see no reason not to use IV magnesium sulfate in these circumstances.

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To the Editor:

We appreciate the comments on our article that was published in CHEST (August 2002), 1 since inhaled ipratropium bromide has been shown by Rodrigo and Rodrigo2 to be useful in adults with severe acute asthma. The methodologies used by previous ipratropium studies involving adults were not sufficient, nor were the results of smaller clinical trials able to document this.3,4 We did not use ipratropium bromide in our protocol because the findings of Rodrigo and Rodrigo2 were published after our study enrollment had been completed.

It is difficult to predict whether the apparent benefit of magnesium would have differed had we added multiple-dose ipratropium to our treatment protocol. It is also difficult to predict whether the results from the ipratropium study would have differed had Rodrigo and Rodrigo2 used magnesium as part of their standard treatment protocol. Since the mechanisms of action of the two agents appear to differ, the benefits might be, to some extent, additive. It is also possible that some patients would respond better to one agent than to the other. The best way to address these questions is through a clinical trial in which a given population (eg, those with an FEV1 < 25% or 30% of predicted) would be randomized to receive ipratropium, magnesium, or a combination of the two interventions.

Regarding the comment that the benefit of magnesium is limited to patients with an FEV1 < 20% of predicted, it is difficult to select a precise cutoff that will predict the response to therapy. We used block randomization techniques or a larger number of patients, we might have been able to identify a more exact treatment threshold. However, we disagree with several statements, particularly those supporting the use of screening chest radiography. Comparisons with the pulmonary complications of HIV infection study of screening chest radiography are not applicable.2 Gold et al1 studied hospitalized patients with constitutional or other symptoms and abnormal chest radiograph findings who were referred for pulmonary consultation. Reviews were of the consultation service ledger rather than of the entire patient record, and pulmonary symptoms may have been missed. Their patients were symptomatic, so the radiographs were not screening studies. Rather, radiographs of patients who are febrile, losing weight, or have extrapulmonary disease are diagnostic tests. In the broadest sense, radiographs in HIV-infected persons who have been admitted to the hospital for other reasons should be considered case-finding studies, not screening studies.

Finally, the observations that both ipratropium and magnesium appear to be beneficial only when there is severe obstruction, as measured by FEV1, presents an important clinical challenge. It is our impression that many patients who are routinely treated in the emergency department do not undergo pulmonary function tests (either FEV1 or peak expiratory flow rate) before treatment. Since FEV1 or peak expiratory flow rate cannot be estimated accurately based on the patient’s appearance, some patients will be undertreated (or overtreated) unless pulmonary function tests are performed. We urge that clinicians adhere to National Asthma Education and Prevention Program guidelines in assessing acutely ill patients in the emergency department.6

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Chest Radiographs in HIV-Infected Persons

To the Editor:

In the May 2002 issue of CHEST, Gold et al1 published an intriguing manuscript reviewing the significance of abnormal chest radiographic findings in HIV-1-infected individuals who did not have specific respiratory symptoms. However, we disagree with several statements, particularly those supporting the use of screening chest radiography. Comparisons with the pulmonary complications of HIV infection study of screening chest radiography are not applicable.2 Gold et al1 studied hospitalized patients with constitutional or other symptoms and abnormal chest radiograph findings who were referred for pulmonary consultation. Reviews were of the consultation service ledger rather than of the entire patient record, and pulmonary symptoms may have been missed. Their patients were symptomatic, so the radiographs were not screening studies. Rather, radiographs of patients who are febrile, losing weight, or have extrapulmonary disease are diagnostic tests. In the broadest sense, radiographs in HIV-infected persons who have been admitted to the hospital for other reasons should be considered case-finding studies, not screening studies.

Statements about our study also question whether a standard diagnostic algorithm was followed and whether diagnoses were missed. In fact, the algorithm was reported, and it included spirometry, diffusing capacity measurements, gallium scans, sputum induction tests, bronchoscopy, and close follow-up at intervals. Clinically significant diagnoses in the 2 months following the abnormal chest radiograph finding would therefore have been captured. The statement that the actual radiographic findings were not reported is also inaccurate.

The reasons for the different findings in both studies include the selection bias of studying hospitalized patients in New York City who are likely to have different demographics and illnesses than the collective group of outpatient, asymptomatic HIV-infected persons. A diagnostic approach that includes chest radiography is probably justified in any hospitalized patient with