Communications for this section will be published as space and priorities permit. The comments should not exceed 350 words in length, with a maximum of five references; one figure or table can be printed. Exceptions may occur under particular circumstances. Contributions may include comments on articles published in this periodical, or they may be reports of unique educational character. Please include a cover letter with a complete list of authors (including full first and last names and highest degree), corresponding author’s address, phone number, fax number, and e-mail address (if applicable). An electronic version of the communication should be included on a 3.5-inch diskette. Specific permission to publish should be cited in the cover letter or appended as a postscript. CHEST reserves the right to edit letters for length and clarity.

Communications to the Editor

Missing the (Acu) Point

To the Editor:

Varon et al (May 2002),1 in an editorial accompanying the study of acupuncture in asthma by Shapiro et al (May 2002),2 commended the study for being “... important because it provides the rigor of Western scientific method to an alternative medical therapy,”7,11 p 1390. In what follows, we would like to call the reader’s attention to at least three potential critical flaws in the design and analysis of the study that render its overall validity and generalizability questionable.

First, the fidelity and integrity of the study intervention rested entirely on the relative competency and proficiency of a single “certified and experienced”2, p 1397, acupuncturist who evaluated the study subjects, diagnosed their condition, and treated the study subjects according to the principles of traditional Chinese medicine (TCM). This, however, is an undesirable research practice since it poses plausible threats to both the construct and external validity of a study, particularly when it fails to reject the null hypothesis.2 Likewise, it would be inappropriate to draw any generalized causal inferences about the efficacy of a surgical procedure or a given method of psychotherapy by examining the outcomes of any single surgeon or therapist, respectively. Negative findings in such studies could arguably be explained as type II error (ie, concluding that there is no effect when in fact there really is an effect), especially when other research indicates opposite results. This is all the more so in TCM research, in which the diagnosis and treatment rests solely on the practitioners’ clinical skills. For this reason, it has been recommended recently6 that studies that evaluate traditional systems of medicine should involve multiple practitioners. Unfortunately, the inclusion of only one acupuncturist in this study also precludes the possibility of testing the hypothesis that the study failed due to suboptimal provision of care, since, from a generalizability standpoint, the assessment of the measurement error and variance associated with the therapist facet of the study requires multiple practitioners.5

Second, it may be argued that the negative findings of this study are a result of a significant threat to its internal validity, stemming from another unfortunate flaw in the study design, the intervention itself. The assertion that this study is more rigorous than other studies that have looked at the efficacy of acupuncture in asthma patients because it provided “personalized” (ie, individualized) treatment seems evidence-free, since all the patients received treatments according to fixed time schedules despite the fact that, according to TCM diagnosis, many of them have had different underlying pathologies. Likewise, giving “the first and last sessions . . . to treat acute attacks of asthma, while the second and third sessions . . . to treat the root”2, p 1397 irrevocably depersonalizes the session design and lacks the flexibility of a tailored treatment plan. If true individualization were to occur, then session design, acupuncture point selection, manipulation technique, and treatment schedules should all have been tailored individually to the patient according to his or her underlying TCM etiology and pathophysiology. Of equal concern is the arbitrary length (3 weeks) of the washout period, which is completely evidence-free.

Third, a severe threat to the statistical conclusion validity of the study deserves attention.3 As the authors acknowledged, asthma as an intact Western clinical entity does not exist in TCM. Rather, in TCM, asthma can be diagnosed by the presence of more than five different syndromes. As Wiegent et al6 have suggested, to achieve homogeneity in study samples in complementary and alternative medicine research, ideal designs should involve a double selection procedure; that is, first, a specific conventional diagnosis should be selected, and second, a specific complementary and alternative medicine system diagnosis should be selected from among the multiple possibilities. Nonetheless, the data analysis in the study of Shapiro et al2 was based on overall between-group (ie, either real or sham acupuncture) comparison of means rather than on subgroup (ie, the five TCM syndromes) analysis. Indeed, a quick look at the “family of lines” in Figures 2 and 3 in the study by Shapiro et al2 reveals relatively large variations in the individual responses to asthma that may be accounted for by subgroup differences. Given the five subgroups and the crossover design, we doubt whether the study was adequately powered,2 which is a concern that may raise some ethical considerations.

In conclusion, we paradoxically agree that the study is important, but for exactly opposite reasons than those that the esteemed authors or the editorialists used to conclude that it was important. Confucius, the great Chinese philosopher, was quoted as saying: “Our greatest glory is not in never failing, but in rising every time we fall.” The study by Shapiro et al2 offers an unusual opportunity to educate us all about research design and generalized causal inferences. If we sincerely intend to compare different systems of medicine, we should enable the equal application of each system. Failing to do so may lead us to draw inaccurate conclusions and may deprive us of the potential for additional therapeutics for our patients.

Opher Caspi, MD, MA
University of Arizona, College of Medicine
Tucson, AZ
Elad Schiff, MD
Bnai-Zion Medical Center
Haifa, Israel
Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Ophir Caspi, MD, MA, Research Assistant Professor, Program in Integrative Medicine, Department of Medicine, College of Medicine, The University of Arizona, Health Sciences Center; PO Box 245153, Tucson, AZ 85724-5153; e-mail: ocaspi@ahsc.arizona.edu

REFERENCES

1 Varon J, Fromm RE Jr, Marik PE. Acupuncture for asthma: fact or fiction [editorial]? Chest 2002; 121:1387–1388
8 Halpern SD, Karlawish JHT, Berlin JA. The continuing unethical conduct of underpowered clinical trials. JAMA 2002; 288:358–362

To the Editor:

The use of alternative medicine techniques in patients with asthma remains unproven and poorly tested. In a recent article in CHEST, Shapira et al (May 2002) reported on their randomized, double-blind, sham-controlled, crossover study of short-term acupuncture in patients with moderate persistent asthma. Drs. Caspi and Schiff raise concerns about the methodology of this study, particularly the use of a single acupuncturist in the delivery of therapy. Certainly, this raises the concern of the generalized applicability of the conclusions of the study. However, the advantage of using one or a few experienced practitioners is that one can expect homogeneity and reproducibility in the treatment.

The correspondents are also concerned about the “personali zed” treatment program. It is their contention that the use by Shapira et al of a fixed time schedule for treatment “depersonalized the session design,” which may have impacted the outcome of the trial. We will leave the defense of this particular design to the authors of the study. However, some structure is required for the practical implementation of any clinical trial.

We must be cautious in the interpretation of every clinical trial. The generalized ability of the conclusions is dependent on the clinical trial design. Despite its shortcomings, we believe that the study by Shapira et al is important because it brought the rigor of Western scientific methodology to alternative medical therapy. The randomized clinical trial (RCT) allows for the objective and unbiased evaluation of a treatment modality, and, while very few RCTs are flawed, we must guard against dismissing an RCT that does not agree with what we believe or practice. The study by Shapira et al has not answered all questions about the role, if any, of acupuncture in the treatment of patients with asthma. However, given its results, we remain skeptical and cannot recommend acupuncture for the treatment of asthma.

Joseph Varon, MD, FCCP
Robert E. Fromm, Jr, MD, MPH, FCCP
Baylor College of Medicine
Houston, TX
Paul E. Marik, MD, FCCP
University of Pittsburgh Medical Center
Pittsburgh, PA

REFERENCES

3 Varon J, Fromm RE, Marik PE. Acupuncture for asthma: fact or fiction [editorial]? Chest 2002; 121:1387–1388

To the Editor:

I would like to comment on the problems mentioned in the letter of Dr. Caspi.

Indeed, our study had a single acupuncturist. We welcome results from larger-scale studies.

As specified in the article, only the second and third sessions were designed to treat the root cause of the asthma, as diagnosed by traditional Chinese medicine. Interestingly, you haven’t mentioned the importance of the practitioner’s treatment intention. As C’hi Po answers to the emperor in the Nei Ching:

Poor medical workmanship is neglectful and careless and must be therefore combated, because a disease that is not completely cured can easily breed new disease, or there can be a relapse of the old disease . . . the most important requirement in the art of healing is that no mistake or neglect occur.

You claim that 3 weeks of washout are “evidence free.” In fact, there is no scientific basis for any length of washout. However, no washout was used in a crossover study of the effect of acupuncture on allergic rhinitis. Also to be noted is that Zhu and Polus used 3 weeks as a washout period and Malmstrom et al did not expect an effect of acupuncture on bronchial asthma 2 weeks after the termination of treatment. Our results show that no effect was seen after 3 weeks, thus supporting our choice of 3 weeks of washout.

You state that the “family of lines” in Figures 2 and 3 shows great variation that may be accounted for by subgroup variation. I call to your eyes the same variation in the placebo group.

Our results deal with acupuncture treatment for asthma as seen by “Western eyes,” eyes that have no ability to make traditional Chinese medicine diagnosis and thus cannot enjoy the subgrouping suggested by you, and so are inadequately powered. From your letter, I understand that you expect the common pulmonologists and general practitioners to make a Chinese diagnosis with subgrouping, then decide if there are chances of asthmatic relief with acupuncture.

By the way, I am not familiar with any Chinese literature that implies that there is a subgroup of asthma in which acupuncture does not help; could you open my eyes in this matter?
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 War: “Fight, but know where there are deficiencies and deficiencies.” Our study does give an answer to the limited question of the effect of short-term treatment on moderate persistent asthma.

Michael Y. Shapira, MD
Hadassah University Hospital
Jerusalem, Israel

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).
Correspondence to: Michael Y. Shapira, MD, Department of Bone Marrow Transplantation, Hadassah University Hospital, PO Box 12000, Jerusalem, Israel; e-mail: shapiram@hadassah.org.il

REFERENCES

1 Veith I. The yellow emperor’s classic of internal medicine. Taipei, Republic of China: Southern Materials Center, 1982; 150

**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) 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, 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.”

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>
<thead>
<tr>
<th>Initial FEV₁ (predicted)</th>
<th>Baseline</th>
<th>End of Protocol</th>
<th>MD at End (95% CI)</th>
<th>MD, Rodrigo and Rodrigo²</th>
<th>MD, Silverman et al³</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 30% predicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silverman et al</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 126)</td>
<td>22.7 (5.7)</td>
<td>43.5 (18.7)</td>
<td>4.7 (0.3–9.3)</td>
<td>2.6</td>
<td></td>
</tr>
<tr>
<td>Mg (n = 122)</td>
<td>23.1 (4.9)</td>
<td>48.2 (18.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo and Rodrigo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 70)</td>
<td>21.7 (5.2)</td>
<td>43.3 (17.1)</td>
<td>12.0 (5.4–18.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB (n = 60)</td>
<td>21.3 (5.8)</td>
<td>55.3 (20.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–30% predicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silverman et al</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 48)</td>
<td>28.1 (3.6)</td>
<td>53.1 (16.0)</td>
<td>–2.9 (–9.4–3.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg (n = 52)</td>
<td>27.3 (2.2)</td>
<td>51.1 (16.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo and Rodrigo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 18)</td>
<td>27.1 (2.1)</td>
<td>54.2 (18.0)</td>
<td>11.5 (0.0–23.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB (n = 22)</td>
<td>27.4 (1.9)</td>
<td>65.8 (17.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–24% predicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silverman et al</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 32)</td>
<td>22.0 (1.2)</td>
<td>37.9 (12.0)</td>
<td>5.9 (–1.2–13.1)</td>
<td>2.9</td>
<td></td>
</tr>
<tr>
<td>Mg (n = 33)</td>
<td>21.9 (1.6)</td>
<td>43.8 (16.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo and Rodrigo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 32)</td>
<td>22.3 (1.5)</td>
<td>41.8 (17.0)</td>
<td>16.9 (6.6–27.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB (n = 16)</td>
<td>21.6 (1.3)</td>
<td>58.7 (15.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20% predicted</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Silverman et al</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 38)</td>
<td>15.9 (2.5)</td>
<td>33.7 (15.4)</td>
<td>13.6 (4.3–22.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mg (n = 25)</td>
<td>16.3 (2.4)</td>
<td>47.3 (20.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo and Rodrigo</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Placebo (n = 20)</td>
<td>15.0 (3.3)</td>
<td>35.8 (14.2)</td>
<td>17.8 (6.5–29.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IB (n = 22)</td>
<td>15.5 (3.9)</td>
<td>53.6 (20.9)</td>
<td></td>
<td></td>
<td></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.\(^3\)–\(^8\) Recently, this evidence has been included in the management guidelines of asthma exacerbation.\(^3\) Silverman et al\(^1\) recognized that the magnitude of the response to magnesium would differ if additional interventions (eg, 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, \(FEV_1 \leq 50\%\) of predicted; \(n = 180\).\(^2\)) 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 \(FEV_1 \leq 30\%\) 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 \(FEV_1\) compared with control subjects. The patients who were the most likely to benefit from the combined treatment were those with more severe obstruction (ie, \(FEV_1 \leq 30\%\) 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 \(FEV_1\) values from our study (only patients with \(FEV_1 \leq 30\%\) of predicted) with those of the Silverman et al\(^1\) at 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 \(FEV_1\) improvements at the end of the protocol in the three subgroups of patients, and, on the contrary, only patients with the lowest initial \(FEV_1\) (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\(^1\) 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 \(\beta\)-agonists plus IB. Finally, we give tribute to two Uruguayan physicians, Rosello and Pla,\(^10\) who first reported on the treatment of patients with acute asthma using parenteral administration of magnesium sulfate in 1936.

Gustavo J. Rodrigo, MD
Hospital Central de las Fuerzas Armadas
Montevideo, Uruguay
Carlos Rodrigo, MD
Asociación Española Primera en Socorros Mutuos
Montevideo, Uruguay

REFERENCES
2 Noppen M. Magnesium treatment for asthma: where do we stand [editorial]? Chest 2002; 122:396–397
3 Plotnick LH, Ducharme FM. Should inhaled anticholinergics be added to \(\beta_2\) agonists for treating acute childhood and adolescent asthma? A systematic review. BMJ 1998; 317:971–977
5 Stoodley RG, Aaron SD, Dales RE. The role of ipratropium bromide in the emergency management of acute asthma exacerbations: a metaanalysis of randomized clinical trials. Ann Emerg Med 1999; 34:8–18
7 Rodrigo GJ, Rodrigo C. First-line therapy for adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. Am J Respir Crit Care Med 2000; 161:1862–1868

To the Editor:

I thank Drs. Rodrigo and Rodrigo for their comment on the article by Silverman et al,\(^1\) and on my accompanying editorial.\(^2\) I acknowledge their suggestion that anticholinergics might or should have been added to standard therapy in the study by Silverman et al;\(^1\) 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,\(^1\) 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.”\(^3\) The study by Silverman et al,\(^1\) 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.\(^4\) I therefore see no reason not to use IV magnesium sulfate in these circumstances.

Marc Noppen, MD, PhD, FCCP
Brussels, Belgium

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).
Correspondence to: Gustavo J. Rodrigo, MD, Departamento de Emergencia, Hospital Central de las Fuerzas Armadas, Ac 8 de Octubre 3020, Montevideo 11600, Uruguay; e-mail: gurodrig@adinet.com.uy
We appreciate the comments on our article that was published in CHEST (August 2002), since inhaled ipratropium bromide has been shown by Rodrigo and Rodrigo\(^2\) 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 Rodrigo\(^2\) 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 Rodrigo\(^2\) 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 FEV\(_1\) < 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 FEV\(_1\) < 20% of predicted, it is difficult to select a precise cutoff that will predict the response to therapy. We presented data by three subgroups to conveniently represent what our regression analysis had demonstrated, which was that the lower the baseline FEV\(_1\), the greater the response to magnesium. We identified an FEV\(_1\) of 25% of predicted as an important reference point based on data from an earlier study.\(^5\) Had we used block randomization techniques or a larger number of patients, we might have been able to identify a more exact treatment threshold. When the data are plotted out, as the FEV\(_1\) moves toward 25% of predicted, magnesium appears to be less effective, and when the baseline FEV\(_1\) is > 25% of predicted, magnesium does not appear to be effective at all. For this reason, we are comfortable recommending that magnesium be considered when the initial FEV\(_1\) approaches ÷ 25% of predicted.

Finally, the observations that both ipratropium and magnesium appear to be beneficial only when there is severe obstruction, as measured by FEV\(_1\), 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 FEV\(_1\) or peak expiratory flow rate) before treatment. Since FEV\(_1\) 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.\(^6\)

Robert Silverman, MD
Long Island Jewish Medical Center
New Hyde Park, NY

---

Correspondence to: Robert Silverman, MD, Department of Emergency Medicine, Long Island Jewish Medical Center, 270-05 76th Ave, New Hyde Park, NY 11042. E-mail: arsilver@aol.com

References


Chest Radiographs in HIV-Infected Persons

To the Editor:

In the May 2002 issue of CHEST, Gold et al\(^1\) 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 al\(^1\) 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 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...
HIV infection. However, there is insufficient evidence to recommend the use of screening chest radiography in asymptomatic patients.

Roslyn F. Schneider, MD, FCCP
Mark J. Rosen, MD, FCCP
Beth Israel Medical Center
New York, NY

REFERENCES

To the Editor:

We appreciate the insightful comments by Drs. Rosen and Schneider. We agree that direct comparisons to the Pulmonary Complications of HIV Infection study cohort cannot be made due to the numerous differences in methodology noted by ourselves and by Schneider et al.1 A large reason for the discrepancy between the two trials is the specialized nature of our cohort; most of our study subjects were inpatients, the majority in psychiatric or prison wards. However, we would like to clarify several points. First, although initially identified by hospital ledgers, the entire medical record was reviewed for each patient; patients with incomplete data in their medical record were excluded. Each patient had been seen by medical staff of the Bellevue Chest Service, and both a history and physical were available. We are confident, therefore, that these patients truly had an absence of specific pulmonary symptoms.

Second, we agree with Drs. Rosen and Schneider that this study does not support the use of widespread screening chest radiograph (CXR) in HIV-1–infected individuals. We believe that such screening was proven cost ineffective both by the Pulmonary Complications of HIV Infection cohort and by Olson et al.2 However, a directed screening of extremely high-risk individuals, as presented in our study, may still be warranted. Drs. Rosen and Schneider correctly point out that the population of our study is misstated in our article. We are confident, therefore, that these patients truly had an absence of specific pulmonary symptoms.

Finally, an important point of our study is not whether directed screening CXR should be performed in select groups of HIV-1–infected individuals, but rather that an aggressive diagnostic approach should be used to evaluate the abnormality, and such an approach will have a high diagnostic yield. Furthermore, the high incidence of pulmonary tuberculosis has significant public health implications. Last, we wished to provide the clinicians the results of the diagnostic modalities we employed to make the diagnosis. The Pulmonary Complications of HIV Infection trial did mention the radiographic abnormalities present in their cohort; this was misstated in our article.

Timothy J. Harkin, MD, FCCP
William N. Rom, MD, MPH, FCCP
New York University School of Medicine
New York, NY

REFERENCES

Cyclooxygenase-2 Inhibitors in Aspirin-Induced Asthma

To the Editor:

Martin-Garcia et al. (June 2002)³ have indicated the safety of a cyclooxygenase (COX)-2 inhibitor, rofecoxib, in patients with aspirin-induced asthma (AIA). The roles of COX-2 in allergen-induced lung inflammation remain poorly understood. When COX-1-deficient and COX-2-deficient mice are immunized with ovalbumin (OVA), lung inflammation indices (ie, number of cells in BAL fluid, proteins, IgE, and lung histology) are significantly greater in both mice than in wild-type mice.² In contrast, the short-term inhibition of both COX-1 and COX-2 during allergen sensitization in BALB/c OVA-sensitized mice resulted in significantly greater airway hyperresponsiveness and higher levels of interleukin-13 in lung supernatants than was the case in untreated mice that had been OVA-sensitized.³ Although these murine models are not believed to be models of AIA, these two in vivo studies indicate that both the lack of COX genes during development and short-term COX inhibition may exacerbate allergic airway inflammation.

An increase in the release of cysteinyl leukotrienes (Cys-LTs) has been suggested to play a pivotal role in the pathogenesis of AIA. The decrease in prostaglandin E₂ release due to aspirin-induced COX inhibition increases the level of Cys-LTs. A report⁴ has demonstrated that Cys-LT protein is overexpressed in bronchial biopsy specimens from patients with AIA. It also has been documented that the increase in Cys-LT levels following aspirin stimulation is unique to patients with AIA, compared with aspirin-tolerant asthma patients and healthy control subjects.⁵ Therefore, large amounts of COX-2 inhibitor may cause the deterioration of asthmatic symptoms resulting from higher levels of Cys-LT concentrations in patients with AIA. Further careful

www.chestjournal.org

CHEST / 123 / 4 / APRIL, 2003

1317
experimental and clinical studies are needed to establish definitive guidelines for the safe use of COX-2 inhibitors in AIA.

Ken-ichiro Inoue, MD
Hiroisa Takano, MD, PhD
Yutaka Kacuhito, MD, PhD
Hajime Sano, MD, PhD
Toshikazu Yoshikawa, MD, PhD
Kyoto Prefectural University of Medicine
Kyoto, Japan

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Ken-ichiro Inoue, MD, Naka Central Hospital, 1753-1, Iida, Naka-cho, Naka-gun, 311-0134 Japan; e-mail: ken@kk.iij4u.or.jp

REFERENCES


To the Editor:

We thank Dr. Ken-ichiro et al for their comments regarding our article that was published in CHEST [June 2002].1 After going through the content of the letter, we would like to highlight that aspirin-induced asthma (AIA) is not mediated by allergic mechanisms but by the shared pharmacologic actions of aspirin and other nonsteroidal antiinflammatory drugs (NSAIDs).2 So, the murine models of ovalbumin-induced bronchial hyperresponsiveness in mice with cyclooxygenase (COX)-1 and/or COX-2 knockout are not appropriate models of NSAIDs. We agree that the biosynthesis of cysteinyl leukotrienes is up-regulated in AIA, but it is not clear that large amounts of COX-2 inhibitor may cause deterioration of asthmatic symptoms in patients with AIA. Rofecoxib was found to be well-tolerated by AIA patients and did not appear to cause asthmatic attacks in patients with AIA and NSAID-induced asthma.

Miguel Hinojosa, MD
Cristina Martin-Garcia, MD
Hospital Ramon y Cajal
Madrid, Spain

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Miguel Hinojosa, MD, Department of Allergology, Hospital Ramon y Cajal, Carretera de Colmenar km 9, 28034 Madrid, Spain; e-mail: mhn011m@saludalia.com

REFERENCES


Talc Pleurodesis vs Iodopovidone

To the Editor:

The report by Olivares-Torres et al (August 2002)1 is an important first step in seeking a safe, inexpensive alternative method to talc for treating patients with pleural effusions by pleurodesis using iodopovidone. The numbers and results are quite similar to those in our 1991 report2 on thoracoscopic talc poudrage (TTP) in which we found a 100% success rate at 1 year when the occurrence of trapped lung was eliminated from the data (which Olivares-Torres et al did a priori). There were no instances of ARDS in our 39 patients or in 360 cases of TTP reported by my mentors.3 Since the calculated incidence of ARDS after talc is on the order of 2 to 1 in 140 patients,4 it would require a study involving thousands of patients treated with iodopovidone pleurodesis to prove that it is safer than talc pleurodesis. Dornicycline and bleomycin pleurodesis have been reported in relatively few patients compared to talc pleurodesis, yet both have been associated with catastrophic respiratory failure.5 Ideally, a prospective randomized study will be performed.

The 9% incidence of ARDS referenced by Olivares-Torres et al did a priori. There were no instances of ARDS in our 39 patients or in 360 cases of TTP reported by my mentors.3 Since the calculated incidence of ARDS after talc is on the order of 1 in 700 to 1 in 140 patients,4 it would require a study involving thousands of patients treated with iodopovidone pleurodesis to prove that it is safer than talc pleurodesis. Dornicycline and bleomycin pleurodesis have been reported in relatively few patients compared to talc pleurodesis, yet both have been associated with catastrophic respiratory failure.5 Ideally, a prospective randomized study will be performed.

The 9% incidence of ARDS referenced by Olivares-Torres et al did a priori. There were no instances of ARDS in our 39 patients or in 360 cases of TTP reported by my mentors.3 Since the calculated incidence of ARDS after talc is on the order of 2 to 1 in 140 patients,4 it would require a study involving thousands of patients treated with iodopovidone pleurodesis to prove that it is safer than talc pleurodesis. Dornicycline and bleomycin pleurodesis have been reported in relatively few patients compared to talc pleurodesis, yet both have been associated with catastrophic respiratory failure.5 Ideally, a prospective randomized study will be performed.

The 9% incidence of ARDS referenced by Olivares-Torres et al did a priori. There were no instances of ARDS in our 39 patients or in 360 cases of TTP reported by my mentors.3 Since the calculated incidence of ARDS after talc is on the order of 2 to 1 in 140 patients,4 it would require a study involving thousands of patients treated with iodopovidone pleurodesis to prove that it is safer than talc pleurodesis. Dornicycline and bleomycin pleurodesis have been reported in relatively few patients compared to talc pleurodesis, yet both have been associated with catastrophic respiratory failure.5 Ideally, a prospective randomized study will be performed.
Olivares-Torres et al. do not describe a simpler alternative to TTP. They injected iodopovidone in conjunction with thoracoscopic pleurodesis in 40 of the 52 patients (77%) in their study. They applied the iodopovidone under general anesthesia in 67% of their patients. General anesthesia is expensive, possibly hazardous, and has been shown to be unnecessary in performing TTP.

TTP required a mean length of stay in our hospital of only 3.9 days. What was the length of stay in this study of iodopovidone? The 30-day mortality rate after pleurodesis is often reported as >10% due to the presence of advanced malignant disease and other comorbidities. The absence of any 30-day mortality rate in the series by Olivares-Torres et al. suggests a very cautious selection of candidates.

Although the use of iodopovidone for pleurodesis presents an interesting possibility, this study does not justify injecting iodopovidone either via chest tube or via thoracoscopic at this time, except in a prospective study protocol.

Yossef Aelony, MD, FCCP
Sancho Palos Verdes, CA

REFERENCES
4 Sahn SA. Talc should be used for pleurodesis. Am J Respir Crit Care Med 2000; 162:2023–2024
7 Aelony Y. Treatment of mesotheliomatous pleural effusion: experimental therapy versus thoracoscopic talc poudrage; pro-talc poudrage therapy. J Bronchol 2001; 8:54–59

To the Editor:

I thank Dr. Aelony for his comments on our article in CHEST (August 2002) and appreciate the opportunity to respond. There are a few points in his letter that need clarification.

1. Safety of talc. For decades, talc, whether by poudrage or slurry, has been considered to be the most effective pleurodesis agent available. Unfortunately, there is growing concern regarding the safety of talc administered intrapleurally. In his letter, Dr. Aelony states that the calculated incidence of ARDS in patients undergoing talc pleurodesis ranges from 0.14 to 0.07% (ie, barely 1 case of ARDS per 1,000 patients treated with talc pleurodesis). However, in the editorial used as reference for these data, the author actually presents an estimated incidence of 7 cases of ARDS per 1,000 patients treated with talc pleurodesis. As we mention in our article, the reported rate of ARDS associated with talc pleurodesis has been as high as 9%. There are at least 32 cases in the literature of ARDS occurring after the administration of intrapleural talc. In eight instances, the patient died. It seems that an important factor in the development of ARDS associated with talc pleurodesis is the size of the talc particle. Although the risk of mesothelioma from talc pleurodesis is very small, the fact that the possibility exists provides another reason not to use talc for pleurodesis, especially in nonmalignant conditions. Iodopovidone has been extensively used in Mexico for almost 10 years without reports of any serious side effects. Obviously, it should not be used in the presence of a bronchopleural fistula. Its passage into the bronchial tree could be associated with the development of ARDS, due to the low pH of talc.

2. Pain and hypotension. Dr. Aelony expresses concern over the report that three of our patients experienced severe pain and hypotension. The use of any effective pleural irritant, including talc, can and will produce intense pleuritic pain (and a vasovagal reaction) if analgesia and anesthesia are inadequate. The control of pain should be individualized, especially in patients with neoplastic diseases, who already are receiving high doses of narcotic analgesics.

3. Need of thoracotomy. Thoracotomy was performed in 40 of our 52 patients with the purpose of obtaining pleural tissue for diagnosis. When malignancy was reported, pleurodesis with iodopovidone was performed at the end of the surgical procedure. However, pleurodesis with iodopovidone can be perfectly and successfully carried out through a tube thoracostomy. The median length of stay in the hospital after pleurodesis was 2 days.

4. Iodopovidone should not be used, except in a prospective study protocol. A controlled clinical trial of pleurodesis using iodopovidone in the study group, and talc in the control group, would involve the use of a substance (talc) that has been associated with a highly lethal complication (ARDS) vs another equally effective substance not yet associated with any serious complications. Besides the ethical dilemma for the investigators, undoubtedly it would be extremely difficult to obtain written informed consent from potential participants.

Rafael Laniado-Laborín, MD, MPH, FCCP
San Ysidro, CA

REFERENCES
2 Sahn SA. Talc should be used for pleurodesis [editorial]. Am Rev Respir Crit Care Med 2000; 162:2023–2024
3 Light RW. Talc should not be used for pleurodesis [editorial]. Am Rev Respir Crit Care Med 2000; 162:2024–2026
Alcoholic Cardiomyopathy and Ventricular Arrhythmias

To the Editor:

We read with interest the article by Piano et al.1 (May 2002) about alcoholic cardiomyopathy (ACM), with a complete clinical and physiopathologic overview on this leading cause of nonischemic heart failure. We agree with all the comments and conclusion of the author, and we thank Dr. Piano for the several citations of our work published in 2000.2 We would like to add a short comment on the problem of ACM and arrhythmias since this issue remains unclear. Alcohol intake is associated with biological changes, such as potassium depletion that may induce arrhythmogenesis. Our work was one of the very few that took into account some arrhythmia risk markers in the evaluation of ACM. Acute consumption of alcohol is a well-known etiology of paroxysmal atrial arrhythmias3,4 with the so-called “holiday heart syndrome,” but there is little information concerning the prevalence or incidence of ventricular arrhythmias in ACM. We found that the prevalence of atrial arrhythmias and of sustained or nonsustained ventricular tachycardia (VT) was not significantly different in either group of patients with idiopathic cardiomyopathy (IDCM) or ACM. A study has found that late ventricular potentials on signal-averaged ECG in long-term alcoholics without preexisting heart disease was associated with more severe steatosis, suggesting that this method could detect early alterations in the myocardium.5 However, we found no difference in the prevalence of late ventricular potentials on signal-averaged ECG in patients with ACM and IDCM.

Currently, our database includes 194 patients with nonischemic dilated cardiomyopathy: 119 patients with IDCM and 75 patients with ACM. Among the latter, we observed 47 patients with complete or almost complete alcohol abstinence and 28, respectively, without alcohol abstinence with a mean ± SD follow-up (FU) of 51 ± 42 months. We now have information on the occurrence of major arrhythmic events during FU (sudden death, sustained VT, ventricular fibrillation [VF]) that we did not published in our initial work of 2000. Figure 1 shows the actuarial curves of events (14 sudden deaths, 10 sustained VT/VF) for the three groups of patients. These data confirm that the prognosis appears similar concerning this aspect of the prognosis for patients with IDCM and ACM without abstinence, and appears much better for patients with ACM and abstinence (only 2% of events during FU).

Therefore, alcohol intake does not seem to worsen prognosis on ventricular arrhythmias by comparison to IDC; however, alcohol abstinence in ACM is associated with a very good prognosis concerning the risk of sudden death, which may be related to the improvement of the left ventricular function. This is further argument to suggest that an aggressive approach to alcohol cessation is needed in these patients.

Laurent Fauchier, MD, PhD
Centre Hospitalier Universitaire Trousseau
Tours, France

Figure 1. Survival curves of sudden deaths and major arrhythmic events (sustained VT, VF) in patients with ACM and IDCM. The solid line indicates patients with ACM and alcohol abstinence, the small dashed line indicates IDCM, and the large dashed line indicates patients with ACM without abstinence. Compared to patients with ACM and alcohol abstinence, relative risk of events was 8.0 for patients with ACM without abstinence (log-rank test, p = 0.01) and 7.3 for patients with IDCM (log-rank test, p = 0.03).

5 Pochmalski G, Genest M, Jibril H. Late ventricular potentials and heavy drinking. Heart 1997; 78:165–169