
To the Editor:

We appreciate the comments on our article that was published in CHEST (August 2002), 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 presented data by three subgroups to conveniently represent what our regression analysis had demonstrated, which was that the lower the baseline FEV1, the greater the response to magnesium. We identiﬁed an FEV1 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 FEV1 moves toward 25% of predicted, magnesium appears to be less effective, and when the baseline FEV1 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 FEV1 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 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 acute 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 al3 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, spu- tum induction tests, bronchoscopy, and open 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.

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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 done 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 much different from that observed in other screening trials. While it is true that CXR should be obtained as a case finding study for those subjects with significant extrapulmonary disease and constitutional symptoms, and these subjects comprised a large percentage of our subjects, only 24% had constitutional symptoms. Furthermore, 40% of our subjects were admitted only for psychiatric reasons or had a CXR as a screening modality. Most who had received a screening CXR were prisoners and were admitted only for evaluation of their abnormal CXR findings. Since patients with psychiatric illnesses and prisoners are usually admitted only for evaluation of their abnormal CXR findings, it is likely that this explains some of the differences between our study and theirs.

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 clinician 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.

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Cyclooxygenase-2 Inhibitors in Aspirin-Induced Asthma

To the Editor:

Martin-Garcia et al (June 2002)1 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

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