**To the Editor:**

We welcome the comments of Dr. Lipworth regarding the comparison between exhaled nitric oxide (NO) and methacholine reactivity in separating doses of inhaled steroid. Our study looked at the short-term effects of administering doses, increased weekly, of inhaled beclomethasone on exhaled NO and PC_{20} methacholine, in a small number of asthmatic subjects.

First, there are important differences in the time courses of response of these two measures of asthma outcome. Exhaled NO is a rapidly responding marker, as seen in a previous study of ours where the maximal fall of NO after 1,000 μg inhaled beclomethasone was complete after only one week. This was the basis for selecting periods of 1 week for each dose level in this study. Thus, it is difficult to compare exhaled NO with PC_{20} methacholine, where the maximal response takes several months.

Second, we agree that, with dose intervals of 1 week, there may have been carry-over effects from the previous dose. We mentioned this in the “Discussion” section.

Third, it is true that, in all subjects combined, the exhaled NO response plateaus at 400 μg, while in the publications referred to by Dr. Lipworth, PC_{20} methacholine plateaus at 1,600 μg. However, because the potential for a parameter to change depends on its absolute value, exhaled NO plateaus at > 800 μg/dl in those subjects with very high baseline exhaled NO, as shown in Figure 1 of our manuscript. Our study is limited, however, by a small number of subjects.

A dose-response relationship for an asthma outcome measure could lead to the ability to tailor the dose of inhaled steroids. Because exhaled NO reacts rapidly, this could be performed in a short period, whereas with PC_{20} methacholine, several months might be necessary.

Before closing the chapter comparing dose responses between exhaled NO and PC_{20}, there is a need to perform further studies of inhaled steroid dose-response in a larger number of subjects, looking at exhaled NO and PC_{20} methacholine over longer periods of time, while controlling for baseline values as covariates.

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**REFERENCE**


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**Severe Centrilobular Emphysema in a Patient Without Airflow Obstruction**

*To the Editor:*

Emphysema is a pathologic diagnosis that often accompanies the clinical finding of chronic airflow limitation. Although these two components often coexist, they may not necessarily progress in synchrony. We report a patient with severe smoking-related centrilobular emphysema and hypoxemic respiratory failure, whose pulmonary function was normal except for a low diffusing capacity of the lung for carbon monoxide (DL_{CO}).

An 81-year-old white woman, a 30-pack-year ex-smoker, had progressive and marked exertional dyspnea, and resting hypoxemia requiring supplemental oxygen. She was slightly overweight with no chest wall deformity and no clubbing. Breath sounds were normal with no wheezes and only few inspiratory crackles in both bases. There was an accentuated pulmonic component of the second heart sound but no evidence of left- or right-heart failure.

Expiratory flow rates were normal (FEV₁, 1.3 L [108%]; FVC, 2.0 L [107%]). Lung volumes via dilution were all slightly elevated. DL_{CO} was severely reduced, at 4 mL/mm Hg/min (23%). The expiratory flow-volume loop is shown in Figure 1. Chest radiographic findings were normal. Radionuclide ventilation-perfusion lung scan findings were low probability for thromboembolism, and ultrasound revealed patent leg veins. Resting room air blood gases showed the following findings: PaO₂, 52 mm Hg; PaCO₂, 37 mm Hg; arterial oxygen saturation, 88%, which decreased to 78% following a brief walk. Hemoglobin level was 16.6 g/dL. High-resolution CT scan (HRCT) showed diffuse centrilobular emphysema, with no bullae or interstitial disease (Fig 2). Home oxygen therapy was continued, and treatment with inhaled bronchodilation was initiated in attempt to improve her dyspnea. She remained in clinically stable condition and was oxygen dependent.

This case is unusual in that emphysema was severe enough to cause marked dyspnea, resting hypoxemia, and a severely reduced DL_{CO}, despite normal chest radiographic findings, normal expiratory flows, and near-normal static lung volumes. Since this is physiologically possible but clinically uncommon, other causes of dyspnea, hypoxemia, and decreased DL_{CO} were considered and excluded.

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**Figure 1. Expiratory flow-volume curve.**
The classic teaching holds that emphysema causes loss of elastic recoil and thereby “functional” airways obstruction. Although emphysematous airspace destruction commonly occurs with airflow obstruction, the two are not interdependent processes.1-3 Results of the HRCT of the chest correlate well with histologic emphysema4,5 and have helped to identify patients with emphysema but not airflow obstruction. To our knowledge, other reported patients have had mild clinical disease, without resting hypoxemia. This patient is unusual because of the severity of her symptoms and hypoxemia, despite normal expiratory airflow. This patient demonstrates that although emphysema and airflow limitation commonly occur together, they are actually separate disease processes.

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Industry and Professional Medical Societies

To the Editor:

I share the concerns of Varkey, as given in “Time for Introspection” (April 2001).1 While commercialism is rampant in all aspects of our society, it is imperative to look at ourselves as a profession. But what should be done?

I have attended annual meetings of the American College of Chest Physicians, the American Thoracic Society, and other professional societies. I do think that the American College of Chest Physicians, in particular, has done an excellent job in disseminating the information and continuing medical education (CME) that are absolutely necessary for any practicing physician, and the Accreditation Council for Continuing Medical Education has fulfilled the mission as stated.2

But should decisions be based on idealism alone? Should we ban all advertisements and/or sponsorship of any CME once and for all? What do the members of the American College of Chest Physicians think about the total banning of all sponsorship? My brief anecdotal experience suggests otherwise. Idealism may dictate that banning all sponsorship by pharmaceutical agencies will look good in the public view; but pragmatically, survival of CME programs at the current stage may not be feasible.

Why should we scorn the pharmaceutical industry? Are we angry at (jealous of) the huge profits of the pharmaceutical industry? Before we start criticizing the industry as a whole, we should look at the enormous cost of bringing a single drug to the market. Extraordinary medical and legal implications have clearly made it impossible to bring drugs to the market at a far lower cost. Finally, it is the society, as defined eventually by the acts of Congress, that would decide the future of both medicine as well as the pharmaceutical industry. It is time for all of us in the medical profession not to view the pharmaceutical industry as a rival but as a necessary partner in health care.

Let me list the minimum necessary memberships and subscriptions (in my opinion) for a pulmonary critical care physician: American College of Chest Physicians, American Thoracic Society, American Medical Association, American College of Physicians, Society of Critical Care Medicine, New England Journal of Medicine, county and state licensing, etc. How many pulmonologists, intensivists, and internists, in these days of Health Care Financing Administration regulations and high overhead costs, would be willing to take over all the memberships and journal costs. (Those journals, of course, would not take any advertisements from drug companies in any form!)

I believe that anonymous reader surveys will be the best approach for this controversy. The adage “to lean neither to the left nor to the right, but to remain in the center,” is probably best for the American College of Chest Physicians.

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