population, both body habitus and degree of effort expended in PEFR measurement vary widely among patients. We have found that percent predicted PEFRs are much more useful for the individual patient, both in assessing progress of therapy and in objectively comparing severity of respiratory distress with that on previous ED visits. Indeed, even the primary supporting study cited by the authors, that by Nowak et al., cautioned that patients with a body habitus falling outside the norm may benefit from percent predicted PEFR calculation.

In summary, the article by McNamara and Cionni, while suggesting an interesting use of objective data (PEFR), suffers somewhat from its lack of emphasis on other useful information that may be expeditiously obtained in the ED on patients in respiratory distress, namely, clinical and radiographic data. Patients with features of both CHF and CLD may be initially managed without a clear differentiation between the two. In addition, we have had good success with the routine use of percent predicted PEFRs in our ED, and we recommend their use in this setting.

Charles V. Pollack, Jr., M.D., Phoenix

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To the Editor:

Dr. Pollack's remarks are welcome and deserve comment. It is agreed that the history, physical examination, chest radiograph, and medication history are very valuable tools for the clinician in differentiating CHF from acute exacerbations of CLD. The PEFR determination should be viewed as an adjunct to these steps. Previous literature and common experience indicate the potential for confusion of the diagnoses as certain findings overlap, including peripheral edema, jugular venous distention, and the presence of wheezing. Our own study indicated that the medication history alone could not correctly classify 44 percent of the study group. Certainly, as Dr. Pollack states, a chest radiograph is invaluable; however, in many hospitals, especially at night (when many of these patients present), there can be substantial delays in obtaining this study. Additionally, the stimulus for this study was, depending on our results, to eventually examine the usefulness of the PEFR in the prehospital setting, where diagnostic difficulty has been previously documented and where chest radiographs are unavailable.

The suggestion that ambiguous cases be managed with low-flow oxygen and the "safe" combination therapy of a selective β2-agonist and a small dose of loop diuretic is somewhat problematic. Our patients were significantly ill, since the entry criteria included a rating of moderate or severe dyspnea by the physician. They therefore required more aggressive therapy than the above cautious approach. Low-flow oxygen to a patient severely dyspneic from CHF would be dangerous, and most physicians, despite the higher beta-2 selectivity of newer agents, would prefer to avoid undue cardiac stimulation of the patient in CHF. Similarly, a "small dose" of a loop diuretic would have been useless in our CHF patients, and most would want to avoid unnecessary fluid losses in CLD patients. In stable patients with milder dyspnea, if the diagnosis is in doubt, rather than treat both CHF and CLD, a more extensive evaluation including chest radiography can be initiated prior to therapy.

I have no doubt that percent predicted PEFRs are purer and more useful than absolute PEFRs, but certain factors led us to report and to clinically use absolute PEFRs. First, at our institution and many others, there is no respiratory technician immediately available to the emergency center and, as mentioned previously, the ultimate goal of this research was to enhance prehospital care, as well as emergency center care. In closing, our article only suggests the utility of the PEFR as an aid to diagnosis. This utility may be enhanced in situations where the chest radiograph is delayed or unavailable.

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Methotrexate and Asthma

To the Editor:

Methotrexate has been recommended as an effective and safe glucocorticosteroid-sparing agent in "steroid-dependent" asthma. Nevertheless, its efficacy remains controversial.

We report the case of a 54-year-old woman with a history of well-controlled asthma, whose respiratory symptoms reappeared while receiving methotrexate therapy. She was a nonsmoking housewife and had no previous relevant medical background. She was hospitalized on two occasions in 1985 for acute crises, and received oral prednisone from November 1985 to March 1986. Her status dramatically improved while receiving inhaled therapy (salbutamol, disodium cromoglycate, and beclomethasone three times a day), which was progressively reduced and eventually stopped in June 1990. She then remained asymptomatic with regular normal spirometric checks from October 1986 to January 1991. In February 1990, the diagnosis of seronegative rheumatoid arthritis was made, and methotrexate therapy, 10 mg/wk, was instituted. In spite of this treatment, there was a recurrence of the asthmatic symptoms in January 1991, necessitating the reintroduction of inhaled therapy (salbutamol, disodium cromoglycate, and beclomethasone). There was no evidence of interstitial lung disease induced by methotrexate. The patient has been asymptomatic again since September 1991, and her FEV, is 2.280 ml (8,020 ml predicted). However, she needs regular treatment; otherwise, breathlessness reappears.

Commenting on a unique case report of a patient suffering from rheumatoid arthritis, Jones and associates supported the idea that weekly low-dose methotrexate therapy could induce clinical and laboratory features of asthma. In our report, it is not possible to determine whether the recurrence of clinical and spirometric signs of asthma experienced by the patient was simply related to the course of the disease itself, or whether it was induced by methotrexate therapy, as suggested by Jones et al. This raises again the question of guidelines for monitoring asthmatic patients whose condition worsens during methotrexate therapy. Methotrexate in our case was unable to prevent recurrence of chest symptoms,
whereas regular inhaled antiasthmatic therapy succeeded. Finally, there may be a link between rheumatoid arthritis and methotrexate-induced airway obstruction, which perhaps could be demonstrated by including airway responsiveness testing when monitoring rheumatoid arthritis patients on low maintenance doses of this drug.

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New Forceps for Biopsy of Peripheral Airways

To the Editor:

Although functional studies have indicated a principal role of the peripheral airways in the obstructive impairment of pulmonary diseases, there have been few morphologic and biochemical studies supporting this idea. Only indirect evidence from autopsied lungs has been obtained, but it still remains unclear how these findings directly reflect in vivo situations. It may be possible to obtain histologic specimens of the peripheral airways by means of open lung biopsy, but this very invasive procedure has little or no merit in patients, especially those with obstructive pulmonary diseases.

Transbronchial lung biopsy (TBLB) via a flexible bronchoscope is available even for patients with impaired lung function, making it possible to obtain specimens of both the large airways and the alveolar regions. Peripheral airways lack cartilage and are accompanied by muscular pulmonary arteries. Attempting TBLB of peripheral airways with the use of conventional forceps necessarily causes serious or fatal bleeding. Therefore, to date, TBLB using conventional forceps has not been useful for obtaining specimens of peripheral airways for histologic or biochemical examination.

For this reason, we developed new forceps (3 mm in external diameter) for the biopsy of peripheral airways. As shown in Figure 1, we can insert these forceps in the closed position via a flexible bronchoscope using an x-ray television monitor, and then open and close the forceps to cut the airway wall. In this way, we can obtain tissue specimens of peripheral airways without any involvement of the accompanying pulmonary arteries.

Segmental bronchial biopsy using conventional forceps (FB 19C, Olympus, Tokyo) and peripheral airway biopsy using the new forceps (Machida, Tokyo) via a flexible bronchoscope (P10, Olympus, Tokyo) were performed on six patients with stable bronchial asthma (two women and four men, aged 64 ± 4 [SE] years [range, 54 to 80 years]) and three control patients with a coin lesion on a chest radiograph (all men, aged 56 ± 14 years [range, 22 to 80 years]). Using these forceps, we obtained specimens of the peripheral airways large enough for histologic examination without any complications (2 × 3 to 3 × 5 mm).

The biopsy specimens were processed for paraffin sectionings and stained with hematoxylin-eosin and elastic-Goldner's stain. All specimens contained epithelium, basement membrane layer, and submucosal layers with various degrees of cell infiltration. Measurement of basement membrane layer thickness and cell counts in submucosal regions were performed with a digitizing tablet coupled to a computer. The thickness of the basement membrane layers in segmental bronchi from bronchial asthma patients showed significantly larger values than those from the control patients (13 ± 2 μm vs 6 ± 1 μm), whereas there were no significant differences between those from peripheral airways of the bronchial asthma and control patients (7 ± 1 μm vs 6 ± 2 μm). Total cell, lymphocyte, and eosinophil counts from both segmental bronchi and peripheral airways from bronchial asthma patients all showed significantly larger values than those from the control patients.

This preliminary report suggests that a thicker basement membrane is a histologic finding particular to large airways, but not to peripheral airways. Autodiagnostic examination and receptor binding assay of the tissue specimens of peripheral airways in various lung diseases are now in progress. Thus, these newly developed forceps enable us to obtain histologic and biochemical findings about the peripheral airways, and to directly compare various functional data. They will be a powerful tool for the understanding of the obstructive impairment in lung diseases.

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Figure 1. New forceps for biopsy of peripheral airways. Forceps can be inserted via a flexible bronchoscope in closed position and then opened and closed to obtain a tissue specimen.