To the Editors: I read with great interest the recent article by Roberts and colleagues (1). Of concern was the marked lymphocytosis present in lavage fluid before irradiation, as well as the slightly elevated cell count. The patients had an increased total cell count (22.4 × 10^6 cells with 61% macrophages, 34.5% lymphocytes, and 4% neutrophils). Such an increase in cellularity and prominent lymphocytes represents a markedly abnormal baseline. In studies reviewed by the bronchoalveolar Lavage Cooperative Group Steering Committee, total cell counts were generally less than 16 × 10^6 cells in nonsmoking patients when the lavage volume was less than or equal to 150 mL. The percentage of lymphocytes in bronchoalveolar lavage fluid in normal persons is universally less than 20% (10% on average). In normal smokers, the total cell count is generally increased on the order of 30 to 50 × 10^6 cells, with lymphocytes not expected to exceed 8% (2).

This finding suggests a baseline lymphocyte alveolitis before any radiotherapy that was apparently exacerbated by a course of unilateral thoracic irradiation.

Determining the cause of this baseline abnormality in these patients is essential before concluding anything about the true effect of unilateral thoracic irradiation. These findings could be associated with methotrexate pneumonitis (3) or toxicity from another chemotherapeutic agent, or they could be secondary to intrinsic allergic alveolitis (4) related to a humidifier system or related to another antigen in the local environment. Studying bronchoalveolar lavage fluid obtained before chemotherapy, as well as screening the patients for hypersensitivity pneumonitis, would be helpful to clarify the underlying disorder.

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References

In response: Both letters comment on the apparently high percentage of lymphocytes in the pretherapy group (1). These lymphocyte percentages are due to important methodologic variables and not to another underlying abnormality. In our study, the pre-radiotherapy cell total number (22.4 ± 15.9 million) and proportion of lymphocytes (34.5% ± 13.4%) before radiotherapy did not differ significantly from the values for normal persons (34.7 ± 19 million and 29.1% ± 12.9%, respectively) (2), which we have determined in other studies (2, 5).
I question the validity of their interpretation that a decreased rate of decline of prebronchodilator FEV<sub>1</sub>, indicates improvement in the unfavorable course of obstructive airway disease seen with bronchodilators alone. Spirometric evidence for irreversible airflow obstruction, which develops at an accelerated rate in asthmatic patients, is best determined after maximal bronchodilator therapy (3). Therefore, analysis of postbronchodilator FEV<sub>1</sub>, rate of decline should be a more realistic reflection of the rate of change of maximal airway function than measurement of prebronchodilator FEV<sub>1</sub>.

To illustrate this point, I have added postbronchodilator FEV<sub>1</sub> slopes to Figure 3 of the article by Dompeling and colleagues (2). They interpreted their figure as indicating that inhaled steroids may double the time before low levels of lung function are reached (Figure 1). As can be seen from the redrawn figure, their theoretical comparison requires that prebronchodilator FEV<sub>1</sub> be greater than postbronchodilator FEV<sub>1</sub>, after year 8 or 9. This result occurs because the rate of decline in postbronchodilator FEV<sub>1</sub> was actually greater after initiation of inhaled steroids (-120 mL/year) than before treatment with inhaled steroids (-98 mL/year). This paradox casts doubt on the validity of their extrapolation.

It is well established that therapy with inhaled corticosteroids improves asthma symptoms. The study of Dompeling and colleagues (2) showed decreased bronchial hyper-reactiveness in asthmatics and alleviation of symptoms and a decrease in the number of exacerbations in both asthmatics and patients with COPD, thus supporting this role for inhaled steroids. I suggest that the improvements in prebronchodilator FEV<sub>1</sub> found in their study probably relate to these changes in bronchial hyper-reactivity, symptoms and exacerbations of asthma and COPD, rather than to the irreversible inflammatory damage that presumably underlies accelerated declines in maximal FEV<sub>1</sub>, noted among asthmatic patients.

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References