Airway Inflammation and Peribronchiolar Attachments in the Lungs of Nonsmokers, Current and Ex-smokers

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Abstract. To determine the effect of smoking cessation on the number and type of inflammatory cells in the walls of the small airways, we examined the lungs of 13 lifetime nonsmokers, 25 patients who had stopped smoking for at least 6 months, and 49 current smokers. We found that, compared to nonsmokers, both ex-smokers and current smokers had significantly increased numbers of total inflammatory cells and polymorphonuclear leukocytes in the walls of the membranous, but not the respiratory bronchioles. These differences were found even when there was no emphysema present in the gross lung specimen, and current and ex-smokers were matched with the nonsmokers for age. The current and ex-smokers had similar numbers and types of inflammatory cells in the airway wall, and in both current and ex-smokers there was no difference in inflammatory cell number or type when the groups were subdivided based on emphysema score less than or greater than 5. Analysis of peribronchiolar alveolar attachments showed an increase in percentage of alveoli destroyed associated with an increased interalveolar distance in both the current and ex-smokers, which did not change with the presence of emphysema. Pulmonary function was similar in the current and ex-smokers, and the group with emphysema showed greater functional abnormalities compared to the group with little or no emphysema.

We conclude that the cigarette smoking habit induces a stereotypical inflammatory response in the small airways. This inflammatory response does not abate after smoking cessation, and in this cross-sectional study, appears to be independent of the presence or absence of emphysema, but related to destruction of the peribronchiolar alveolar attachments.

Key words: Airways—Inflammation—Smoking.

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Introduction

The idea that cigarette smoke induces an acute inflammatory reaction in the airways and lung parenchyma is well accepted. Bronchopulmonary lavage has shown that there are increased numbers of both total inflammatory cells and polymorphonuclear leukocytes (PMN) in the airway lumens and alveoli of cigarette smokers [14], and analyses of the peripheral blood have shown that cigarette smokers have a leukocytosis [3, 16]. Although examination of the peripheral blood in ex-smokers has shown white cell counts in the range of nonsmokers, bronchopulmonary lavage studies have either not included, or not separated ex-smokers as a specific subgroup. Therefore, although one would intuitively expect that pulmonary inflammation would abate, there are no data to support this conclusion.

Using a semi-quantitative grading system, we have previously examined airway inflammation in current and ex-smokers and found that there was no difference between the groups [20]. This system does not, however, provide true quantitative results of inflammatory cell numbers or types, and it is possible that smoking cessation is associated with a decreased number of polymorphonuclear leukocytes.

Emphysema is most likely the end result of an imbalance of the protease-antiprotease balance within the lung [7], and it is possible that inflammation in the airway wall, induced by cigarette smoking, adds to the proteolytic burden. If the inflammatory response to cigarette smoke acts as a continuum, subjects with emphysema might have a greater inflammatory cell population in the airway walls. Alternatively, it is possible that the inflammatory cell proteases affect only the adjacent alveolar walls, resulting in peribronchiolar alveolar destruction.

To answer these questions, we studied a group of patients who were undergoing lung or lobe resection.

Materials and Methods

Subjects

The patient population consisted of 13 lifetime nonsmokers, 25 ex-smokers, and 49 current smokers; there were 31 women and 56 men. An ex-smoker was defined as a subject who had ceased smoking more than 6 months prior to surgery. Patients who clinically, or on the surgical specimen, had either large tumors or obstructive pneumonia beyond an endobronchial tumor were not included in this study.

Pulmonary Function Data

The patients were studied less than 1 wk prior to surgery. Expiratory flow maneuvers were performed using a 9L Steadwell spirometer or a Collins computerized spirometer. Functional residual capacity (FRC) was measured with the helium dilution technique. Forced expiratory volume in 1 sec (FEV1) was expressed as percent predicted using the formula of Morris and