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The Cells of Asthma

Eosinophils, lymphocytes, and mast cells are generally recognized as the central cellular orchestrators of airway inflammation within most conceptual models of asthma. Based on clinical correlates, these models may be broadly grouped into those that focus on an atopic pathogenesis or nonatopic pathogenesis of airway inflammation. Many definitions of “atopy” are utilized, but in general, the atopic models are clinically characterized by the presence of positive skin test reactions to known allergens in a pattern consistent with IgE-mediated reactions. The nonatopic models lack the skin test reactivity to allergens and, by implication, IgE is thought to be less important in the inflammation pathogenesis.1 To a variable extent, both models incorporate the same effector cells and the same soluble mediators.

The cellular variability and overlap of the two models are exemplified by a study of atopic and nonatopic patients in which the cellular content of sputum was examined at two time points: during an asthma exacerbation and 2 weeks following treatment.2 The investigators found that the sputum content of eosinophils varied nearly 100-fold among the patients at each time point. However, all patients, including the nonatopic patients, had a decrease in the sputum content of eosinophils following corticosteroid therapy. While these observations may simply reflect a noncausal pharmacodynamic effect of the steroid therapy, another interpretation of the findings is that...
even “low” levels of airway mucosal eosinophilia may have clinical consequences in some patients.

The potential impact of relatively small amounts of airway mucosal eosinophilia is especially important when considering the findings of Gibson et al in this issue of CHEST (see page 1329). These investigators examined induced-sputum cytology among patients with mild, moderate, or severe persistent asthma. There was an extensive variation in the proportion of eosinophils within the sputum, such that some patients within each severity category could be classified as either “eosinophilic” or “noneosinophilic.” In exploratory analyses, the investigators compared certain characteristics of the eosinophilic asthma patients to the noneosinophilic patients and to healthy volunteers. These comparisons resulted in the observation that noneosinophilic asthma patients had a greater content of neutrophils within their sputum than either the eosinophilic patients or the healthy control subjects.

On superficial reading of the findings of Gibson et al, one might conclude that persistent asthma may be divided into an eosinophilic type and a noneosinophilic type. However, close examination of the data shows that such a dichotomous categorization may be inappropriate. When compared to the healthy control subjects, the sputum eosinophil content was approximately sevenfold higher in the noneosinophilic asthma group and 30-fold higher in the eosinophilic asthma group. Similarly, the sputum content of eosinophil cationic protein was approximately 10-fold higher in the noneosinophilic group and 20-fold higher in the eosinophilic group. Hence, both asthma groups had an increased eosinophil content within the airway when compared to healthy control subjects. The inappropriateness of an “all or none” categorization is reinforced by the finding of Gibson et al that pulmonary function and asthma symptoms appeared similar between the two groups. The two groups did appear to differ in the dose of corticosteroid required to control the asthma, with a higher dose required for the group with the highest sputum eosinophil counts. This observation suggests that this eosinophilic group may actually have had somewhat more severe asthma than the group of patients with a lower sputum eosinophil content. Such an implication is consistent with certain findings from endobronchial biopsies of severe persistent asthmatic patients. Wenzel et al1 found that a history of respiratory failure requiring mechanical ventilation was more common among patients with severe asthma having eosinophilic infiltration of the airway mucosa than among patients with much lower mucosal eosinophil content.

The findings of Gibson et al illustrate the large variability in airway content of eosinophils and neutrophils among asthma patients and emphasize the potential utility of induced sputum examination in helping to define the cellular architecture of airway inflammation. The simplicity of the technique may allow the sequential collection of samples over a series of time points. Such sequential analyses may help clarify the interesting finding of Gibson et al of sputum neutrophilia in association with low-level sputum eosinophilia among some patients with asthma.

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Expanding Knowledge of Lung Volume Reduction

Flaherty and coworkers are to be congratulated for their current article in CHEST (see page 1337) on results following lung volume reduction surgery (LVRS). This surgical intervention, reintroduced by Meyers et al,1 provides palliative treatment for patients suffering from end-stage emphysema who have exhausted best medical and physical rehabilitation therapy. Clinical improvement includes relief from dyspnea and oxygen use with increased exercise tolerance, lung mechanics, and improvement in overall quality of life. The improvement in expiratory airflow and reduction in hyperinflation has been attributed to the increase in lung elastic recoil, following resection of the worst emphysematous areas. There is subsequent repositioning of the diaphragm with recruitment of inspiratory muscles of respiration,2–5 which can now operate more effi-