patients, the weighted mean proportion of subjects with eosinophilic inflammation was 51%, the rest being noneosinophilic asthma [3]. In most of the studies with noneosinophilic asthma, the predominant cells were neutrophils associated with increased levels of interleukin-8 [4–6] and similar cellular and inflammatory profiles as in occupational asthma [2]. Asthma of all grades of severity can have neutrophil dominance in the airways [3], thus establishing it as a variant of asthma, not just a marker of severity. This is unlikely to be the effect of inhaled corticosteroids as shown by two studies [2, 6].

Eosinophilc asthma is CD4/interleukin-5 driven in response to an allergen, whereas neutrophilic asthma is usually mediated by interleukin-8 triggered by viral infection, pollution or bacterial endotoxin [3]. It is important to try to differentiate between these two groups, which may have implications on treatment, and it is tempting to postulate that inhaled corticosteroids will not be as effective in patients with noneosinophilic asthma. Future studies should be directed to prospectively evaluate any prognostic difference between these two groups of asthma.

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From the author:

I appreciate the comments made by S. Mukherjee and S. Basaki about my article on similarities and differences between asthma and chronic obstructive pulmonary disease (COPD) [1]. As they rightly point out, an increase in eosinophils is not necessarily characteristic of severe asthma or of an exacerbation of asthma. They stress the importance of trying to differentiate between eosinophilic and noneosinophilic asthma.

My article was dealing with the major characteristics that help to differentiate between asthma and COPD and how these affect the response to pharmacological agents. The teaching point here was that the different responses to inhaled anti-inflammatories seen in asthma and COPD may have their basis in differences in the cell populations in the two diseases. I emphasised that COPD is not one disease but rather a spectrum of diseases. The same can be said for asthma, which is remarkably heterogeneous.

Clearly, we need more information about the heterogeneity of the inflammatory response in asthma. The prevalence of noneosinophilic asthma varies from study to study, and the reason for this variability has been attributed to patient or disease characteristics, such as severity or control of asthma, smoking, age, medication use, stage of exacerbation and recent exposure to allergens or environmental pollutants [2]. Understanding the pathology better will require much more information based on biopsies obtained in these different circumstances.

The practical clinical question is whether we can differentiate between eosinophilic and noneosinophilic asthma (or between those who respond to anti-inflammatories and those who do not) using clinical criteria or simple clinical tests. Although not yet a simple clinical test, analysis of bronchoalveolar lavage fluid or induced sputum has received a lot of scrutiny recently in the hope that this can be used to distinguish responders from nonresponders. To date, the answer is not clear. One recent study that supports the use of sputum eosinophils to adjust treatment was reported by GREEN *et al.* [3]. These investigators followed 74 asthmatic patients for 12 months to see if the number of exacerbations was higher in patients randomised to a treatment algorithm based on normalising the sputum eosinophil count *versus* those randomised to management by British Thoracic Society Guidelines. They reported that treatment directed at normalising the induced sputum eosinophil count reduced the frequency of exacerbations without the need for additional anti-inflammatory therapy. In another study, GODON *et al.* [4] measured sputum eosinophilia before and after treatment with inhaled corticosteroids in 51 mild, uncontrolled, steroid-naïve asthmatics. Of these, 29% had an eosinophil count $\leqslant 1\%$. Baseline characteristics of this group and the group that had an eosinophil count of $>1\%$ were not different and neither was the response to 1 month of inhaled corticosteroid treatment, as judged by symptoms, quality of life, forced expiratory volume in one second and methacholine responsiveness. Studies like these are helping to answer the important question of whether sputum eosinophils can be used as a clinical tool to predict the response to treatment or titrate treatment.

The important point is that we recognise the heterogeneity of asthma (and chronic obstructive pulmonary disease) and continue to look for simple clinical tools that can help to differentiate groups that respond to different pharmacological agents. This will require well-designed and adequately powered clinical trials.

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