Recent studies of the bronchial mucosa of patients with mild asthma have firmly established asthma as a chronic inflammatory disease characterised by an airway submucosal infiltration of lymphocytes and eosinophils, epithelial shedding and subepithelial reticular fibrosis. There is increasing evidence that cytokines are involved in the chronic airways inflammation of asthma and increased expression of mRNA for certain cytokines has been demonstrated in bronchial biopsies obtained from patients with mild asthma [1, 2]. Increased expression appears to relate to the clinical severity of the disease and can also be induced by allergen challenge [3]. Because of the predominant enhanced expression of mRNA for cytokines that are usually expressed by T-helper type 2 (Th2) lymphocytes e.g. IL-3 and IL-5 and a reduction in the profile of cytokines produced by Th1 lymphocytes (e.g. interferon-γ), it has been suggested that the inflammatory reaction in asthmatic airways is a manifestation of Th2 non-asthmatics, &rained peripheral mononuclear cells and in bronchial biopsies obtained from normal subjects, atopic non-asthmatics and 1/8 mild asthmatics and 4/9 moderately severe asthmatics. Following 70 cycles of amplification, there was a greater percentage of positive expression for IL-5 mRNA in the atopic non-asthmatics, mild asthmatics and moderate asthmatics, but no increase in positive expression in the normal subjects (1 out of 8). For GM-CSF mRNA for which there was no expression in any of the biopsies from all the groups after 35 cycles of PCR, there were 3/7 and 4/9 positive responses in the mild and moderate asthmatics groups respectively, compared to 1 for each of the normal and atopic groups. There was also some degree of increased expression in the 2 atopic groups for IL-2 mRNA. There were no differences in expression of the other cytokines studied.

Using polymerase chain reaction, we have shown that a range of cytokine mRNA can be detected in buffy coat cells and in endobronchial biopsies obtained from normal subjects, atopic non-asthmatics and asthmatic patients. Thus, buffy coat cells from normal subjects commonly express IL-1, IL-2, IL-8 and TNF-α, while in endobronchial biopsies, there is generally a lower frequency of expression with a maximum of 2 out of 8 normals expressing IL-1, IL-2 and TNF-α. Of interest, increasing the number of cycles of amplification from 35 to 70 cycles did not increase the frequency of positive expression for these cytokines.

In terms of differences between the groups, we found that there was a high degree of expression of IL-5 equally amongst the groups for the peripheral blood mononuclear cells. However, there was a greater expression of IL-1, IL-8 and TNF-α in the moderate-severe asthmatics when compared to the other 3 groups. This suggests that these cytokines in the peripheral mononuclear cells may be markers of severity of asthma. However, this is not confirmed by the endobronchial biopsy data which show a clear difference between normals who in general do not express IL-5 mRNA, and the other 3 groups who showed high levels of expression following 70 cycles of PCR amplification. Thus, IL-5 mRNA was associated with the atopic state and is not a marker of the absence or presence of asthma. In addition, atopic asthmatics in the group of asthmatics needing steroid therapy also expressed IL-5 mRNA. A more clear-cut marker for asthma in endobronchial biopsies appear to be GM-CSF mRNA which was observed in 7 out of 16 asthmatics but only in 1/7 atopic and 8/9 normals after 70 cycles of PCR. There was less clear-cut signals for TNF-α and IFN-α. In contrast to the results of peripheral blood mononuclear cells, none of the cytokines tested appear to indicate severity of asthma. Our result indicate that there are more important differences in the patterns of expression of cytokines in endobronchial biopsies compared to that of buffy coat cells; thus, more information is likely to be obtained from an examination of results of endobronchial biopsies.

Using in-situ hybridisation, increased expression of IL-1, IL-4, IL-5 and GM-CSF has been demonstrated in bronchial biopsies of patients with asthma but not the presence of IFN-γ, supporting the hypothesis that inflammation is associated with the activation of Th2 cells. These cytokines have been localised to activated T cells. The increase in IL-5 mRNA was observed in patients with symptomatic but not asymptomatic asthmatics. In addition, GM-CSF mRNA expression in lymphocytes increases following allergen challenge of asthmatic subjects. Our data show that in asthmatics irrespective of their clinical severity, there was expression of IL-5 and to a lesser extent of GM-CSF, supporting the hypothesis of a Th2 mRNA cytokine profile in asymptomatic controlled asthmatics. Also, of support, is the relatively low level of expression for IFN-γ mRNA, a Th-1 cytokine, which was not different from that observed in normal subjects. On the other hand we found very little expression of IL-3 and IL-4 mRNA in endobronchial biopsies even after 70 cycles of PCR. This data suggests that the Th2-type cytokine expression seen in these subjects is associated with the presence of atopy rather than asthma as previously described.

References: