Determinants of Asthma Severity

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Key Words

Asthma severity

Determinants

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Bronchial asthma, irrespective of the presence of atopy, is characterised by a cellular infiltrate, with eosinophils being the most prominent and typical finding in this disease. Studies to date have focused on mild to moderate asthma, but even in mild forms of the disease, the extent of cellular infiltration, such as the number of eosinophils, has been shown to correlate with physiological indices of disease activity. We have studied the bronchial inflammatory cell infiltrate in subjects suffering from atopic asthma of varying severity and of subjects suffering from intrinsic asthma as judged by skin test reactions to common aero-allergens. By comparison with the normal state, and irrespective of the presence of atopy, increased numbers of activated eosinophils and mast cells were found to be a feature of this disease. In mild asthma, a small percentage of bronchial T lymphocytes (media 10%) retrieved by bronchoalveolar lavage were activated, as indicated by surface interleukin (IL)-2 receptor (IL-2R) expression, increasing further with natural exposure to pollen allergen in sensitive individuals and decreasing after treatment with inhaled corticosteroids. In keeping with increased T cell activity, BAL T cells in asthma had increased proliferative responses to mitogens and anti-CD3, although by comparison with T cells from nor-

mals and T cells from blood in general these were less dependent on IL-2. In contrast, severe, steroid-dependent asthma was shown to be a distinct entity, with disease activity and high serum IgE levels being maintained despite the reduced numbers of mucosal T cells, mast cells, eosinophils, and cells immuno-staining for IL-4. The striking feature of severe asthma was a 10-fold increase in the percentage of activated (CD25+) T cells in the mucosa, consistent with their resistance to corticosteroids. In addition, the intensity of immunohistochemical staining for IL-5 was increased in severe asthma. Preliminary studies of mRNA transcription in biopsies of severe patients have shown persistent activation of genes localised on

chromosome 5, in particular those encoding for IL-5, which possibly explains the persistent eosinophilia that is seen in the bronchial mucosa of these patients despite the use of high doses of anti-inflammatory drugs.

Taken together, our studies indicate a prominent role for mast cells, eosinophils and T cells in asthma pathogenesis and point to a major role for T cells in the severe form of the disease. However, it is apparent that the extent of infiltration with cells is less important than their activity.

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