

Images in Allergy and Immunology

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Effects of steroids on inflammation and cytokine gene expression in airway inflammation

Editor's note: This new feature, Images in allergy and immunology, is designed to highlight the current concepts of immunopathology of allergic diseases and other common immunologically mediated diseases. The presentation takes the form of sets of images that involve cross-pathology, histopathology, and molecular pathology.

In the first few Journal issues in which it appears, this feature will focus on asthma. Other topics to be addressed (in subsequent issues) include allergic rhinitis, sinusitis, atopic dermatitis, food allergy, and immune deficiency.

Corticosteroid drugs are very effective in the treatment of allergic inflammation, including asthma and rhinitis. In general, steroids improve airway inflammation by reducing inflammatory cell infiltrate and by promoting cellular apoptosis. In steroid-sensitive indi-

INFLAMMATORY CELLS

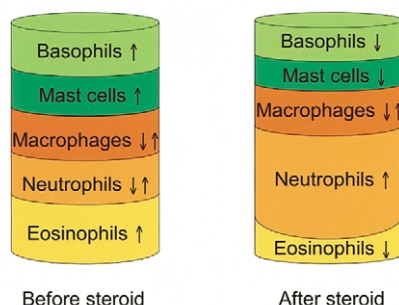


FIG 1. Inflammatory cells before and after treatment with corticosteroids in airway inflammation. There is a decrease in the number of eosinophils, mast cells, and basophils.

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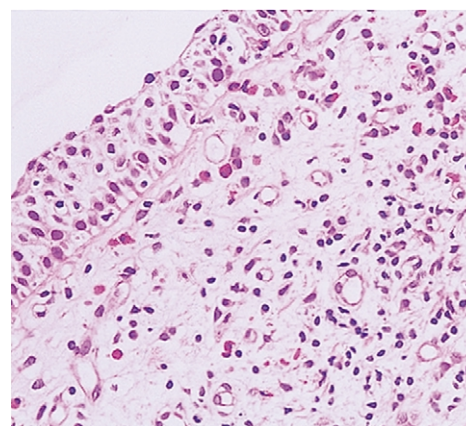


FIG 2

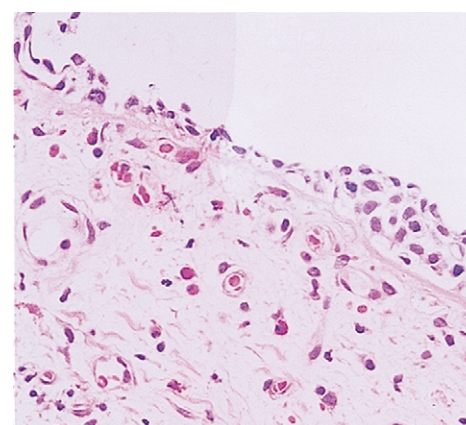


FIG 3

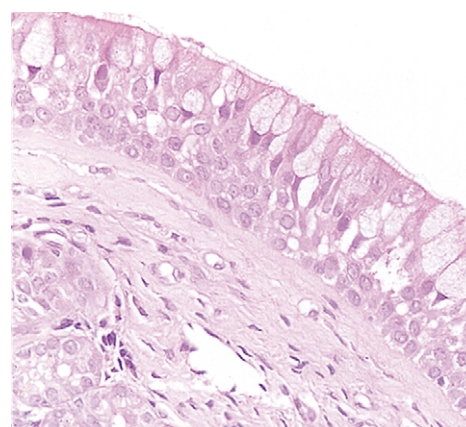


FIG 4

FIGS 2-4. Biopsy specimens from the upper airways show an increase in the inflammatory cells, particularly eosinophils (Figs 2 and 3), which decrease significantly after treatment with steroids (Fig 4). Note also the squamous metaplasia (Fig 2) and the detachment of the epithelium (Fig 3). Although not in all cases, prolonged treatment with steroids might restore normal phenotype (Fig 4).

viduals, steroids reduce the number of eosinophils, mast cells, and basophils in the airway (Figs 1, 2, 4, 5, and 6). There are conflicting reports on the effect of steroids on the numbers of macrophages and T cells in the airways of asthmatic individuals; however, most of

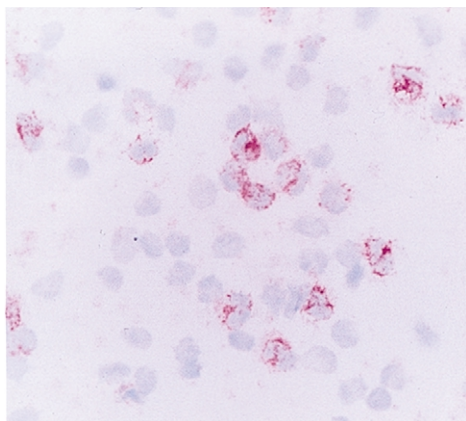


FIG 5

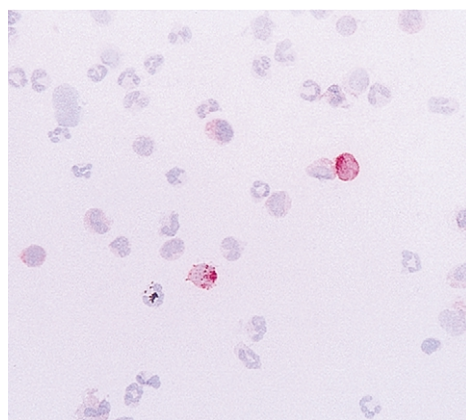


FIG 6

FIGS 5-6. Eosinophils could be detected through use of a noninvasive method in sputum preparation (Fig 5); treatment with corticosteroids is associated with a decrease in the number of eosinophils in sputum (Fig 6).

CYTOKINES - Steroid sensitive

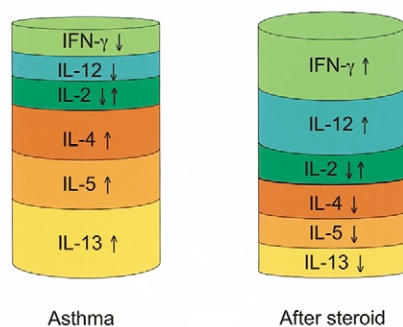


FIG 7. The effect of steroids on cytokine gene expression in steroid-sensitive patients.

the reports suggest that steroids are effective in reducing the activation status of these cells. In contrast, steroids have been reported to increase the number of neutrophils in steroid-sensitive individuals in both the central and the peripheral airways (Fig 1). Cytokine and chemokine genes are very sensitive to steroids in

CYTOKINES - Steroid resistant asthma

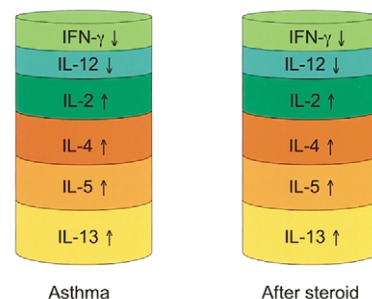


FIG 8

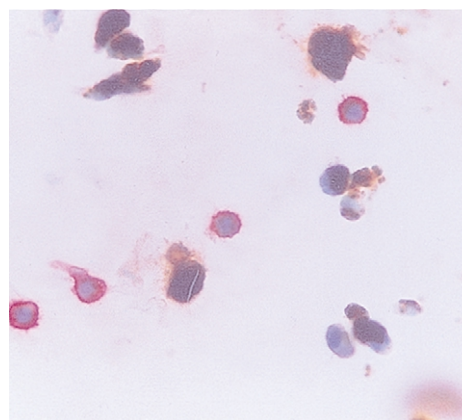


FIG 9

FIGS 8-9. Inability of steroids to inhibit cytokine gene expression in asthmatic individuals showing a high level of IL-2 and IL-4 expression in steroid-resistant asthma (Fig 8). This could lead to upregulation of GR β (Fig 9), which is detected in bronchoalveolar lavage preparation.

CHEMOKINES - Asthma

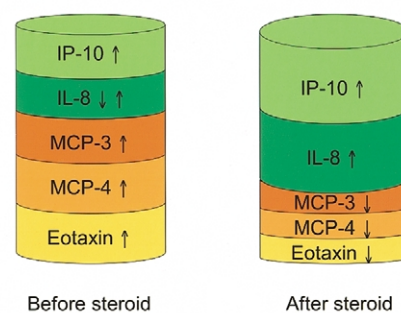


FIG 10

general. In vivo, the use of steroids is associated with differential downregulation of T_H2 cytokines (IL-4, IL-5, and IL-13), but it might upregulate T_H1-like cytokines, including IFN- γ and IL-12 (Fig 7). Very few studies to date have examined the effect of steroids on chemokine expression in asthma. Recently

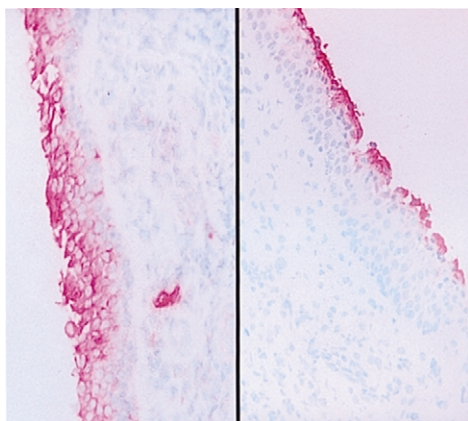


FIG 11

FIGS 10-11. Effect of corticosteroids on chemokine gene expression (Fig 10), with an example of MCP-4 immunoreactivity in the epithelium before and after steroids (Fig 11).

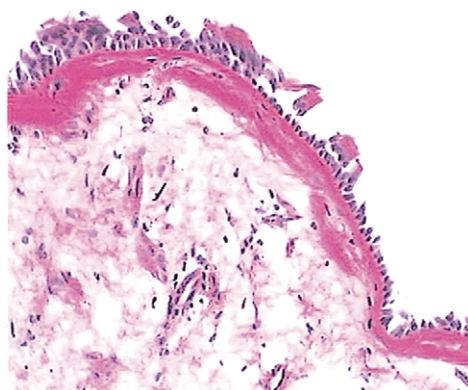


FIG 12

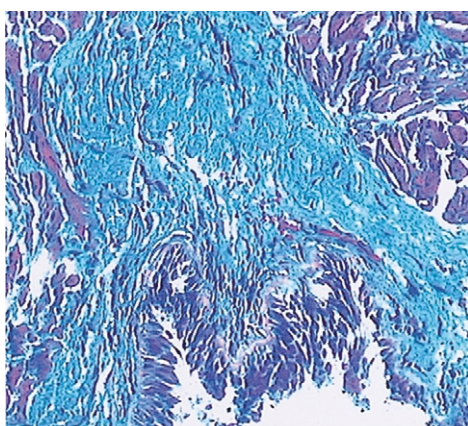


FIG 13

FIGS 12-13. Steroids have no or little effect on subepithelial fibrosis or smooth muscle mass. Shown are a collagen staining in endobronchial biopsy after prolonged treatment with inhaled steroids (Fig 12) and a Masson Trichrome staining of an endobronchial biopsy specimen from an asthmatic patient after steroid treatment (Fig 13), illustrating persistent increase in subepithelial fibrosis and an increase in smooth muscle mass.

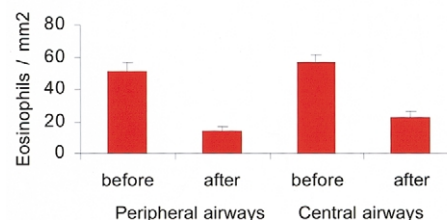


FIG 14

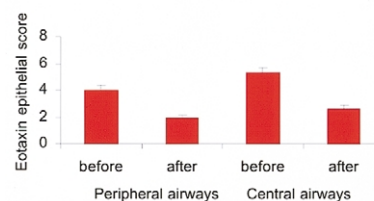
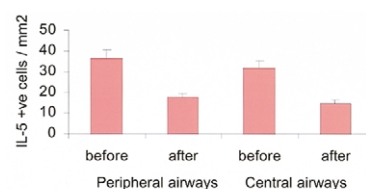


FIG 15

FIGS 14-15. Inhaled steroids (HFA preparation) have the ability to be deposited in peripheral airways, where they can decrease eosinophil numbers (Fig 14) as well as the expression of eotaxin and IL-5 (Fig15).

it has been demonstrated that steroids downregulate eotaxin and other eosinophil-associated chemokines but have little effect on IL-8 and IP-10 (Figs 10 and 11). In general, steroids have no or little effect on structural changes associated with airway remodeling. Their effect on the airway epithelium is controversial. In the upper airways, steroids can restore the epithelium to normal phenotype (Figs 3 and 4). Steroids have no effect on reducing the subepithelial fibrosis even after prolonged treatment with inhaled steroids (Fig 12). Although steroids were reported to have an effect on airway smooth muscle function, their effect on the smooth muscle mass is not clear. Steroids can also inhibit goblet cells hyperplasia and decrease vascularity and permeability associated with inflammation.

Next in the series *Images in allergy and immunology*: Eosinophils in allergic inflammation