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Asthma is now one of the most common chronic diseases in Western countries and is characterized by reversible airway obstruction, bronchial hyperresponsiveness and airway inflammation. For many years, anti-inflammatory therapy in asthma has been largely reliant on glucocorticoids (GCs) – particularly in their inhaled form – and their use is associated with a striking reduction in the numbers of activated eosinophils, mast cells, and T cells in vivo. However, although GCs can be efficacious, they are also rather nonspecific in their actions and may not be of benefit to patients with severe asthma who experience virally-induced exacerbations of their disease. Their use also raises concerns regarding side effects and compliance particularly in children and adolescents. Furthermore, even in cases of good compliance, patients with moderate and severe asthma may experience significant residual symptoms including exacerbations of their disease that in some cases can be life-threatening (Walsh 2006). There is therefore a clear need for the development of more effective and targeted therapy for asthma.

Allergic asthma is the most common form of the disease and is characterized by elevated titres of specific immunoglobulin E (IgE) to common environmental allergens. Thus, one approach to asthma therapy is to block the effects of IgE. Omalizumab is an anti-IgE monoclonal neutralizing antibody that binds IgE at the same site (Cε3 domain of the Fc fragment) as the IgE high affinity receptor (FcεRI) expressed by mast cells and basophils. This results in inhibition of degranulation and synthesis of newly generated chemical mediators by IgE-sensitized mast cells and basophils. In the current issue of *Therapeutics and Clinical Risk Management*, Gennaro D'Amato and colleagues have provided a comprehensive review of the use of omalizumab in the treatment of allergic asthma. Careful analysis of published clinical trials by the authors reveals positive benefits on asthma symptoms together with a corticosteroid sparing effect, reduced use of bronchodilators and improved quality of life in patients with asthma. Importantly, omalizumab is effective in those patients with severe persistent allergic asthma that is inadequately controlled by currently available asthma medication. Interestingly, it appears that in addition to its direct effects on basophils and mast cells, omalizumab also inhibits activation of eosinophils, T lymphocytes, and B lymphocytes which are fundamental to the chronic inflammatory response in allergic diseases such as asthma. The authors' conclusion is that omalizumab offers both therapeutic and economic value and represents a major advance for the treatment of patients with inadequately controlled severe persistent allergic asthma. Omalizumab appears to be well tolerated with few side-effects reported in published studies. However, more long-term studies are needed to fully elucidate the benefit and safety of anti-IgE therapy in asthma.

Many mediators contribute to the pathophysiology of asthma thus development of specific antagonists directed at these substances represents an attractive target for inflammation resolution. However, it is unlikely that a single antagonist will have a major clinical effect compared with nonspecific agents such as corticosteroids. Indeed, strategies to block a single mediator such as PAF antagonists, thromboxane inhibitors, and bradykinin antagonists have all proved to be disappointing (Barnes 2000). The cysteinyl leukotrienes (LTC_4, LTD_4, and LTE_4) induce bronchoconstriction and are highly potent mediators of airway inflammation. The cysteinyl leukotriene receptor

antagonists were the first new class of anti-asthma drugs to be introduced in the last 30 years and are now an established part of the treatment of adult asthma. Overall, they are less effective than inhaled corticosteroids but some patients show a striking improvement and a corticosteroid-sparing effect has been demonstrated (Lipworth 1999). Three drugs of this class are in use at present: zafirlukast, pranlukast, and montelukast. All three are specifically active against the cysteinyl leuko-trienes by blocking their receptor, CysLT1.

References

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