

Introduction

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In 1999, the European Federation of Allergy and Airways Diseases Patients' Associations (EFA) determined that almost one-quarter of the population of Europe, which corresponds to 80 million people, suffers from allergic rhinitis and/or asthma (1). Worldwide, the prevalence of allergy and asthma continues to increase, as documented in adults by the European Community Respiratory Health Survey (ECRHS) (2) and in children by the International Study of Asthma and Allergies in Childhood (ISAAC) (3). Dramatic geographic variations in prevalence clearly implicate lifestyle and environmental factors in this disturbing trend. Pollution, diet, standards of hygiene, childhood infections, a rural vs. urban environment, and climate are among the factors proposed to interact with a genetic predisposition for allergic respiratory disease (4–10). There have been major decreases in emissions of principal air pollutants in Europe in the past 20 years – a 68% reduction in sulphur dioxide and 25% reduction in both nitrogen oxides and nonmethane volatile organic compounds (11). However, it is likely that the increased prevalence of respiratory allergy is related to multiple environmental factors, the elimination of which may be difficult, if not impossible, to achieve on a population-wide basis.

Allergic disease negatively affects the individual and society via impairment of health-related quality of life, decreased work efficiency and school performance, increased absenteeism, and increased healthcare costs. Allergic rhinitis causes fatigue, poor health perception, compromised social function, learning impairment, anxiety, family dysfunction, and sleep disturbance (12,13). In a survey of European patients with respiratory allergy, high percentages complained of limitations in daily activities, such as climbing stairs (40%), exercise (55%), gardening (44%), housework (35%), shopping (26%), and sleeping (50%) (1). Chronic

urticaria, a common dermatological disease with significant mast cell/basophil-mediated pathophysiology, causes sleep disruption, fatigue, social isolation, energy loss, and emotional and sexual difficulties (14). Over-the-counter allergy medications with sedative effects can further compromise cognitive and psychomotor functioning, having a negative effect on productivity (15,16). In Europe, allergic rhinitis is estimated to cost billions of euros/dollars (€/€) annually in direct healthcare costs, and indirectly due to loss of productivity. In France alone, allergic rhinitis has been estimated to cost close to €/\$0.5 billion annually in direct medical costs and €/\$1 billion annually through absenteeism from work (17). Asthma costs billions more (18,19). As reported by Professor Van Cauwenberge in this Supplement, the average estimated total direct and indirect costs of asthma annually per patient are approximately €/\$2000–3000 in Europe (20). The Asthma Insights and Reality in Europe (AIRE) survey found that absence due to asthma was reported by up to 27.6% of asthmatic adult workers and up to 52.7% of asthmatic school children (21). Sixteen per cent of surveyed parents of European asthmatic children worry that their child's education may be compromised by absenteeism (22).

Allergic rhinitis is associated with significant comorbidity. In patients with allergic rhinitis, respiratory tissues have increased susceptibility to infection, including sinusitis, otitis media, and respiratory tract infection. Psychological disorders associated with allergic rhinitis include depression and anxiety disorder (23). However, the comorbidity of allergic rhinitis and asthma may be the most significant scientifically because it has resulted in a quantum shift in understanding of allergic respiratory disease and of allergy in general. Respiratory allergy is now recognized as a disorder of the entire respiratory tract, with different manifestations in the specific target organs of the nose and lungs.

Recognition of the relationship between allergic rhinitis and asthma has been formalized by new diagnostic terminology – combined allergic rhinitis and asthma syndrome (CARAS). There are also recommendations for 1) total airway evaluation in the presence of either persistent allergic rhinitis or persistent asthma and 2) a total airway-treatment strategy that combines the upper and lower airways in terms of efficacy and safety (24). Perhaps even more importantly, allergy is now recognized as a systemic process, amenable to systemic intervention.

Better understanding of the IgE-dependent allergy cascade has fostered rational drug design; it has also increased knowledge about the mechanisms of action of medications currently available for the treatment of allergic rhinitis. Glucocorticosteroids inhibit the allergy cascade but are not selective for it (25), necessitating the development of targeted delivery systems (e.g. intranasal, inhaled, and topical) to minimize the safety issues associated with systemic administration. Because of inadequate oral absorption, local administration is also necessary for the cromones, which act on mast cells to inhibit histamine release. Local administration may increase the onset of action of histamine H₁-receptor antagonists (antihistamines), but oral administration intervenes systemically in the allergy cascade, providing symptom relief at many target sites. All antihistamines competitively and reversibly block the effect of histamine at its receptor, thereby blocking the early phase of an IgE-dependent allergic reaction and inhibiting the histamine-mediated contribution towards the late-phase response of ongoing allergic inflammation. However, the similarities between antihistamines may be outweighed by differences in tissue delivery and molecular activity (24). For example, most second-generation antihistamines are excluded from the central nervous system, minimizing the undesirable central effects, such as sedation, that are associated with first-generation drugs. Differences between antihistamines in lipophilicity and in tissue deposition may also affect delivery to target sites. Antihistamines also differ in the potency of H₁-receptor antagonist activity and in anti-allergic effects. For example, as described in this Supplement, desloratadine is a once-daily, orally active, nonsedating antihistamine that has potent H₁-receptor antagonist activity, and also inhibits numerous other mediators in the allergy inflammatory cascade (mainly *in vitro*), mediators that are

involved in the late-phase response of chronic inflammation.

As recommended by the evidence-based document Allergic Rhinitis and Its Impact on Asthma (ARIA), written in collaboration with the World Health Organization, oral antihistamines are the first-line treatment of allergic rhinitis, recommended for the relief of both nasal and ocular symptoms (24). Nasal glucocorticosteroids are also recommended in patients with intermittent symptoms that are troublesome, disturbing sleep or impairing activities, although the efficacy of short, repetitive courses has not been demonstrated. Patients with persistent nasal symptoms (e.g. more than 4 days/week for more than 4 weeks) usually suffer from nasal obstruction. ARIA recommends management with nasal glucocorticosteroids because nasal obstruction responds only partially to most antihistamines. The major disadvantages of intranasal administration are suboptimal distribution within the nose, poorer patient compliance than with oral medications, and absence of activity against symptoms at other sites (e.g. ocular). In patients with concomitant asthma symptoms, local administration of glucocorticosteroids should be both nasal and bronchial, which may further decrease compliance with treatment and increase adverse effects. However, there is some evidence that concomitant asthma symptoms may be improved merely by relieving nasal symptoms with nasal glucocorticosteroids, or by the systemic anti-allergic actions of certain oral antihistamines.

As reported in this Supplement to *Allergy*, once-daily administration of desloratadine provides effective and well-tolerated antiallergy activity. In patients with seasonal allergic rhinitis, desloratadine improves nasal, ocular, asthmatic, and dermal symptoms; decreases the use of asthma medication; and improves quality of life. In contrast to most antihistamines, desloratadine significantly reduces the severity of nasal obstruction. In patients with chronic idiopathic urticaria, desloratadine provides rapid and sustained relief of pruritus, reduces the number and size of hives, reduces sleep disturbances, and improves activities of daily living. Desloratadine is nonsedating, nonimpairing, and has an adverse-event profile similar to that of placebo. Thus, once-daily, oral desloratadine offers convenient, well-tolerated, systemic intervention of both the early- and late-phase allergic processes, which manifests as relief of allergic symptoms at multiple target sites and an improvement in quality of life.

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