SUMMARY
The prevalence of allergic diseases such as allergic rhinitis (AR) and asthma is markedly increasing world-wide as societies adopt western life styles. Allergic sensitization is an important risk factor for asthma and AR, and asthma often co-exists with AR. An estimated 300 million people worldwide have asthma, about 50% of whom live in developing countries and about 400 million people suffer from AR. Yet, AR is often under-diagnosed and under-treated due to a lack of appreciation of the disease burden and its impact on quality of life, as well as its social impact at school and at the workplace. However, AR with or without asthma is a huge economic burden. Thus, there was clearly a need for a global evidence-based document which would highlight the interactions between the upper and lower airways including diagnosis, epidemiology, common risk factors, management and prevention. The Allergic Rhinitis and its Impact on Asthma (ARIA) document was first published in 2001 as a state-of-the-art guideline for the specialist, the general practitioner and other health care professionals. Subsequent new evidence regarding the pathomechanisms, new drugs and increased knowledge have resulted in the publication of the ARIA 2008 update. The present review summarizes the ARIA update with particular emphasis on the current status of AR and asthma in the Asia-Pacific region and discusses the Western and Asian perspective.
substantial. However, rhinitis is often under-diagnosed, misdiagnosed and/or under-treated.\textsuperscript{12}

Moreover, many patients with asthma have rhinitis, and rhinitis is a major risk factor for asthma and often precedes it. Increasing evidence on the link between allergic rhinitis and asthma comes from epidemiologic, immunologic and clinical studies. Epidemiologically, up to 40\% of patients with AR also have asthma, and up to 80\% of patients with asthma experience nasal symptoms. Both AR and asthma are chronic inflammatory diseases of the airways and their inflammatory mechanisms are characterized by an inflammatory infiltrate made up of eosinophils, T cells, and mast cells that release several mediators, chemokines and cytokines, inducing local and systemic IgE synthesis, and activate a systemic link via the bone marrow. Studies have shown that patients with AR exhibit bronchial hyper-responsiveness (BHR) and an increase in inflammatory cells, and that a nasal allergen challenge further increases this hyper-reactivity. Results of several retrospective studies indicated, that for patients with asthma the presence of co-morbid allergic rhinitis is associated with higher annual medical costs, as well as an increased likelihood of asthma-related hospital admissions and emergency visits. These findings highlight the potential for improving asthma outcomes by treating co-morbid AR. This link may be due to cross talk between the upper and lower airways, the direct impact of inflammatory mediators released locally and to the systemic link between the two.

Epidemiologic studies done in different parts of the world have consistently shown that asthma and rhinitis often co-exist in the same patients.\textsuperscript{13-16} Adults and children with asthma and concomitant AR experience more asthma-related hospitalizations and physician visits, incur higher asthma drug costs than patients with asthma alone\textsuperscript{17-20} and experience more frequent absences from work and decreased productivity with few exceptions.\textsuperscript{21}

Based on the strength of the above, the first ever evidence-based position paper on rhinitis devoted to the relationship between rhinitis and asthma and its therapeutic implications entitled ARIA: 'Allergic Rhinitis and its Impact on Asthma' emphasizing the importance of treating allergic rhinitis and asthma globally as 'One Airway One Disease' was developed. The ARIA initiative was developed as a state-of-the-art guideline for the specialist as well as for the general practitioner in order to update their knowledge of allergic rhinitis, emphasize the impact of allergic rhinitis on asthma, provide an evidence-based document on the diagnostic methods and an evidence-based revision of the presently available treatments. It clearly proposes a stepwise strategy for the management of allergic rhinitis. Moreover, a new classification is also proposed for allergic rhinitis namely "intermittent" or "persistent" rhinitis based on the duration of the disease and "mild" and "moderate-severe" based on the severity of symptoms and quality of life.

ARIA update

A large number of papers were published since the ARIA was first developed thus extending our knowledge.\textsuperscript{22-27} The ARIA classification was validated\textsuperscript{15,23,26} although some proposed a three level classification of the severity of AR.\textsuperscript{27,28} New evidence on the pathomechanisms, new methods of diagnosis, new drugs, and new evidence on the safety or side effects of existing drugs have been published.\textsuperscript{29-32} Hence, the need to update the ARIA guidelines. The ARIA Update also covers aspects of treatment with complementary and alternative medicine,\textsuperscript{18} sports and rhinitis in athletes,\textsuperscript{19,33,34} the link between rhinitis and asthma in children\textsuperscript{35-39} and specific information on developing countries.\textsuperscript{40-42} The grading of evidence and management recommendations of the ARIA 2008 update used the Shekelle and not the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach.\textsuperscript{43,44} Therefore, recommendations made by the 2008 ARIA update may change once the GRADE approach is incorporated. A stepwise approach for the management of AR is proposed in Fig. 1.

Asthma and allergic rhinitis in Asia Pacific and the Asian perspective

The prevalence of allergic diseases in Asia varied widely but was found to be rising (asthma 29.1\%; AR up to 45\%) mostly in low- and mid-income countries.\textsuperscript{45,46} In Thailand, the prevalence of all three major allergic diseases increased significantly from the ISAAC phase I survey
performed in 1995, *i.e.* asthma increased from 12.2\% to 14.5\%, AR from 37.9\% to 50.6\% and eczema from 9.8\% to 15.7\%.\(^{47}\) In Japan, rhinitis has increased from 3.8\% in 1984 to 32\% and asthma from 4.6\% in 1992\(^{48}\) to 9.1\% (Akasawa A. 2006; unpublished) and more than 42\% of patients with asthma have AR. The prevalence of childhood asthma in Taiwan has increased from 1.3\% in 1974 to 5.07\% in 1985\(^{49}\) and more recently, the overall cumulative and 12-month prevalence of wheezing and rhinitis in the younger children was 8.2\% and 44.4\%, respectively; and in the older children, 6.9\% and 42.2\%.\(^{50}\) Similarly, in Singaporean preschoolers, the cumulative and previous-12-months prevalence of wheezing was 27.5\% and 16.0\%, respectively, and the current asthma and rhinitis prevalence was 11.7\% and 25.3\%, respectively. By contrast, the prevalence of current wheezing, diagnosed asthma and allergic rhinoconjunctivitis in Tibet was 0.8\%, 1.1\%, and 5.2\%, respectively.\(^{51}\) While the asthma prevalence in rural Bangladesh was 16.1\%\(^{52}\) and in Pakistan there was a doubling of the prevalence of AR and asthma in ISAAC III as compared to ISAAC I, a study in urban India presented the overall prevalence of asthma with 2.38\%.\(^{53}\) The prevalence of allergic rhinitis in 5-11yr children in Vietnam was 34.9 \%\(^{54}\) and the prevalence of allergic rhinitis in patients with asthma was 48.54\% (Le Van Khang, *et al.* Study of sensitivity, specificity of house dust mite allergen made in Vietnam for the diagnosis of asthma, Ministry of Health of Vietnam, Jan 2002 to Dec 2004, www.cimsi.org.vn). The asthma prevalence in Australia increased from 8\% in 1989-90 to 11\% in 1995 but the prevalence plateaued in recent years with 2004 prevalence of asthma at 14-16\% in children and 10-12\% in adults (Australian Centre for Asthma Monitoring, www.asthmamonitoring.org).
Although overall regional data for adults are scant, it is estimated that 1-10% have asthma and 10-32% have AR. In a more recent study, the self-reported prevalence of AR in China had wide variations, ranging from < 10% to > 20% with about 15% suffering from persistent AR. More recent data showed an increase in the prevalence of AR in Korea from 6 -10% to > 20% in the adult population. The distribution of the severity of AR was mild intermittent (25.7%), moderate to severe intermittent (16.4%), mild persistent (16.4%) and moderate to severe persistent (41.2%).

Recent data showed a very high co-morbidity of asthma and rhinitis as 60-80% of asthma patients had rhinitis symptoms. The younger asthmatic patients had a higher co-morbidity (80%) than the elderly patients (60%) moreover, asthmatic patients with rhinitis presented more severe clinical symptoms in both adult and children indicating that rhinitis may affect asthma severity and outcome.

Although aeroallergens that trigger allergy and asthma in Asia Pacific vary from area to area house dust mites are the major triggering allergen in most of Asia followed by pollens, insects, molds and fungi.

In a study on patient perceptions of asthma management across Asia, patients reported frequent and unnecessary symptoms and exacerbations because of a lack of adequate asthma control. Twenty-seven percent of adults and 37% of children with asthma reported absences from work or school in the previous year due to asthma, and 40% required hospitalization, emergency department visits, or unscheduled emergency visits to other health care facilities in the previous year. Asthma severity varied, with Vietnam and China reporting the most patients with severe, persistent symptoms. Absenteeism from work was highest in the Philippines (46.6%) and lowest in South Korea (7.5%). In a survey of parents of children with asthma in four Asian countries, most children with asthma (73%) had pre-existing symptoms of AR and asthma with co-morbid AR substantially affecting their quality of life and worsening their asthma symptoms. However, awareness of the co-morbidity of AR and asthma amongst the parents of asthmatic children was only about 50%.

The socio-economic burden via annual costs of treating asthma and AR - both direct costs (hospitalization, medications) and indirect costs (time lost from work, premature death) - are substantial, and represent an even heavier burden in societies with emerging economies. In eight countries in Asia Pacific, the annual per-patient direct costs ranged from US$ 108 to US$ 1,010. Total per-patient costs, including productivity costs, ranged from US$ 184 to US$ 1,189. Urgent care costs were 18% to 90% of the total per-patient direct costs. The total cost of asthma in Singapore was estimated to be about US $33.93 million per annum, based on figures from 1992-1993. Of this amount, US$ 17.22 million was incurred in direct costs and US$ 16.71 million from indirect costs. In-patient hospitalization accounted for the largest proportion of direct costs (approximately US $8.55 million) and loss of work productivity (US $12.7 million) comprised the major proportion of indirect costs. The total medical cost of asthma in Korea was 2.04 billion US dollars in 2004. Direct costs and indirect costs equally contributed to total costs (0.96 and 1.08 billion dollars respectively). If intangible costs (willing to pay method) were included, total costs inflated to 4.11 billion US dollars, which were nearly equivalent to 0.44% of its GDP in 2004.

From the evidence listed in this summary, it is clear that there is a close linkage between asthma and AR. It is therefore recommended that patients with persistent AR should be evaluated for asthma, including appropriate history taking and spirometric parameters, at an early stage. On the other hand, patients with asthma should be evaluated for rhinitis. Unfortunately in reality there is a gap in this practice in many countries in the region. Partly this is due to the lack of allergy medicine as a recognized specialty in some countries as well as to governmental regulations restricting specialists to practice as organ-based specialists. To resolve this problem and to have an integrated therapeutic strategy is one of the major challenges in the Asia Pacific region.

Based on these constraints we also need to consider treatment strategies that can really treat both the upper and the lower airway diseases. Leukotriene receptor antagonists are recommended for patients with both rhinitis and asthma in this ARIA summary. As the only established etiological
treatment for allergic diseases, allergen-specific immunotherapy (SIT) needs to be highlighted as well. Allergen-specific immunotherapy should be considered not only after unsatisfactory traditional pharmacologic treatments but also for patients who have a clear IgE-mediated allergic disease based on history and positive SPT as an early adjunct to standard pharmacotherapy.

Subcutaneous immunotherapy has been found to be effective and safe, and sublingual immunotherapy is now becoming more popular, because of its convenience and lower side effects but the use of standardized vaccines and higher allergen doses (50-200 higher than subcutaneous) in the maintenance stage should be emphasized.

CONCLUSION

The prevalence of asthma and AR is increasing in the Asia Pacific region and the prevalence of co-morbidity is high. The perception of patients and physicians regarding the link between asthma and rhinitis varies between countries, but seems to be higher than expected. However, knowledge is not directly translated into practice since few physicians co-prescribe treatments for rhinitis and asthma in the same patient.

The recommendations of the ARIA workshop in 1999 are still valid, and in particular, it is recommended that all patients with AR, particularly if it is persistent, should be evaluated for asthma. AR is not only a risk factor for underlying asthma but could be a risk factor for asthma exacerbations. Patients with asthma should likewise be evaluated for rhinitis, and a combined strategy should ideally be used to treat the upper and lower airway diseases in terms of efficacy and safety.

REFERENCES


