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► **To cite this version:**

Ruby Pawankar, Chaweewan Bunnag, Nikolai Khaltsev, Jean Bousquet. Allergic Rhinitis and Its Impact on Asthma in Asia Pacific and the ARIA Update 2008. World Allergy Organization Journal, 2012, 5 (Suppl 3), pp.S212. <inserm-00815533>

**HAL Id: inserm-00815533**

**<http://www.hal.inserm.fr/inserm-00815533>**

Submitted on 18 Apr 2013

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# Allergic Rhinitis and Its Impact on Asthma in Asia Pacific and the ARIA Update 2008

Ruby Pawankar,<sup>1</sup> Chaweewan Bunnag,<sup>2</sup> Nikolai Khaltsev,<sup>3</sup> and Jean Bousquet<sup>3</sup>

**Abstract:** The prevalence of allergic diseases such as allergic rhinitis (AR) and asthma are markedly increasing to epidemic proportions worldwide as societies adopt Western lifestyles. An estimated 300 million persons worldwide have asthma, about 50% of whom live in developing countries, and about 400 million people suffer from AR. AR has a marked impact on quality of life, socially, at school, and in the workplace and is a huge socioeconomic burden. Thus, there was clearly a need for a global evidence-based guideline not only for managing AR but also highlighting 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 document for the specialist, the general practitioner, and other health care professionals. Subsequent research and increasing knowledge have resulted in the ARIA 2008 update. The present review summarizes the ARIA update with particular emphasis on the current status of AR and asthma in Asia Pacific.

**Key Words:** allergic rhinitis, asthma, ARIA update, evidence-based, Asia Pacific

(*WAO Journal* 2012; 5:S212–S217)

Allergic rhinitis (AR) is an IgE-mediated inflammation of the nasal mucosa induced after allergen exposure and presents with the 3 cardinal symptoms of sneezing, nasal obstruction, and rhinorrhea. AR is a global health problem that causes major illness and disability worldwide. It affects social life, sleep, school, and work.<sup>1–5</sup> The economic impact of AR is substantial.

More than 400 million patients suffer from AR<sup>6–9</sup> but there are still differences between rural and urban areas, both in developed and developing countries,<sup>8,10–12</sup> possibly because of differences in immune reactions.<sup>13</sup> A large number of patients also suffer from nonallergic rhinitis<sup>14</sup> but the characterization of this disease is unclear as there are many phenotypes of nonallergic rhinitis.

In 2001, the ARIA (Allergic Rhinitis and its Impact on Asthma) World Health Organization (WHO) evidence-based document was published<sup>15</sup> and the statements of evidence for

the development of ARIA followed WHO rules and were based on those of Shekelle et al.<sup>16</sup>

The ARIA document was intended to be a state-of-the-art review for the specialist and for the general practitioner and other health care professionals to update their knowledge of AR, to highlight the impact of AR on asthma, to provide an evidence-based documented revision on the diagnosis methods and the treatments available, and to propose a step wise approach to the management of the disease.

## ARIA UPDATE 2008

As a result of a large number of papers with new information on existing drugs, mechanisms, and newer therapies published during the past 7 years,<sup>17–22</sup> it was important to have an ARIA update.

- The ARIA classification proposed “intermittent and persistent” have been validated,<sup>23–26</sup> although some authors proposed extension of the severity of AR to 3 levels.<sup>27,28</sup> However, because this would not lead to treatment differences, the ARIA experts proposed continuation of the classification of rhinitis severity as “mild” or “moderate/severe.”
- New methods of diagnosis have been proposed for allergic and nonallergic rhinitis.<sup>29–32</sup> The diagnosis of AR is often easy, but in some cases it may cause problems and many patients are still underdiagnosed, often because they do not perceive the symptoms of rhinitis as a disease.
- Furthermore, the gaps in our knowledge in the first ARIA document, which include some aspects of treatment with complementary and alternative medicine,<sup>18</sup> sports and rhinitis in athletes,<sup>19,33,34</sup> and rhinitis and its links with asthma in children,<sup>35–41</sup> have been addressed in the ARIA update.

A large list of treatments was considered in the ARIA 2008 update.<sup>42–44</sup> With respect to pharmacologic treatments, intranasal corticosteroids have been recommended to be the first-line therapy in patients with moderate to severe disease and are also effective on ocular symptoms,<sup>45</sup> H<sub>1</sub> antihistamines are important treatments for all patients, and leukotriene receptor antagonists are particularly important for patients with rhinitis and asthma.<sup>46,47</sup> However, tertiary prevention of allergy is still a matter of debate because clinical trials do not usually show any efficacy of single allergen avoidance measures.<sup>17</sup> Sublingual allergen-specific immunotherapy has proven to be

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a safe and effective treatment,<sup>48-51</sup> but clinical trials need to be standardized.<sup>52,53</sup> An algorithm of the management of AR is provided (Fig. 1). However, there is continuous progress in our understanding of the mechanisms of AR, and novel treatment approaches are constantly published.<sup>54</sup> Nonallergic rhinitis is still a matter of discussion and effective treatment may be difficult.<sup>55</sup>

Another important aspect of the ARIA update was to consider the comorbidities of AR, and in particular asthma. Epidemiologic studies have consistently shown that asthma and rhinitis often coexist in the same patients in every region of the world.<sup>56-59</sup> Most patients with asthma have rhinitis, but the prevalence of asthma in patients with rhinitis still needs to be assessed.<sup>60,61</sup> Adults and children with asthma and documented concomitant AR experience more asthma-related hospitalizations and physician visits, and incur higher asthma drug costs, than adults with asthma alone.<sup>62-65</sup> These

patients also experience more frequent absences from work and decreased productivity. However, some studies have not shown such an association.<sup>66</sup>

Many patients with AR have an increased bronchial reactivity to methacholine or histamine,<sup>67</sup> especially during and some time after the pollen season.<sup>68,69</sup> Nasal and bronchial inflammation are often related,<sup>70</sup> but remodeling of the nose and bronchi seem to differ.<sup>71</sup>

Intranasal treatment of the nose does not considerably impact the lower airways,<sup>72</sup> possibly because the characterization of seasonal asthma needs more insight<sup>73</sup> and most studies have been carried out on this disease. However, some compelling data suggest that new studies with innovative methods need to be initiated.<sup>47,74,75</sup> Oral drugs acting on asthma and rhinitis have an effect on both sites.<sup>46</sup> Research has also shown that the addition of nasal topical corticosteroids to standard asthma treatment reduces severe exacerbations of asthma by

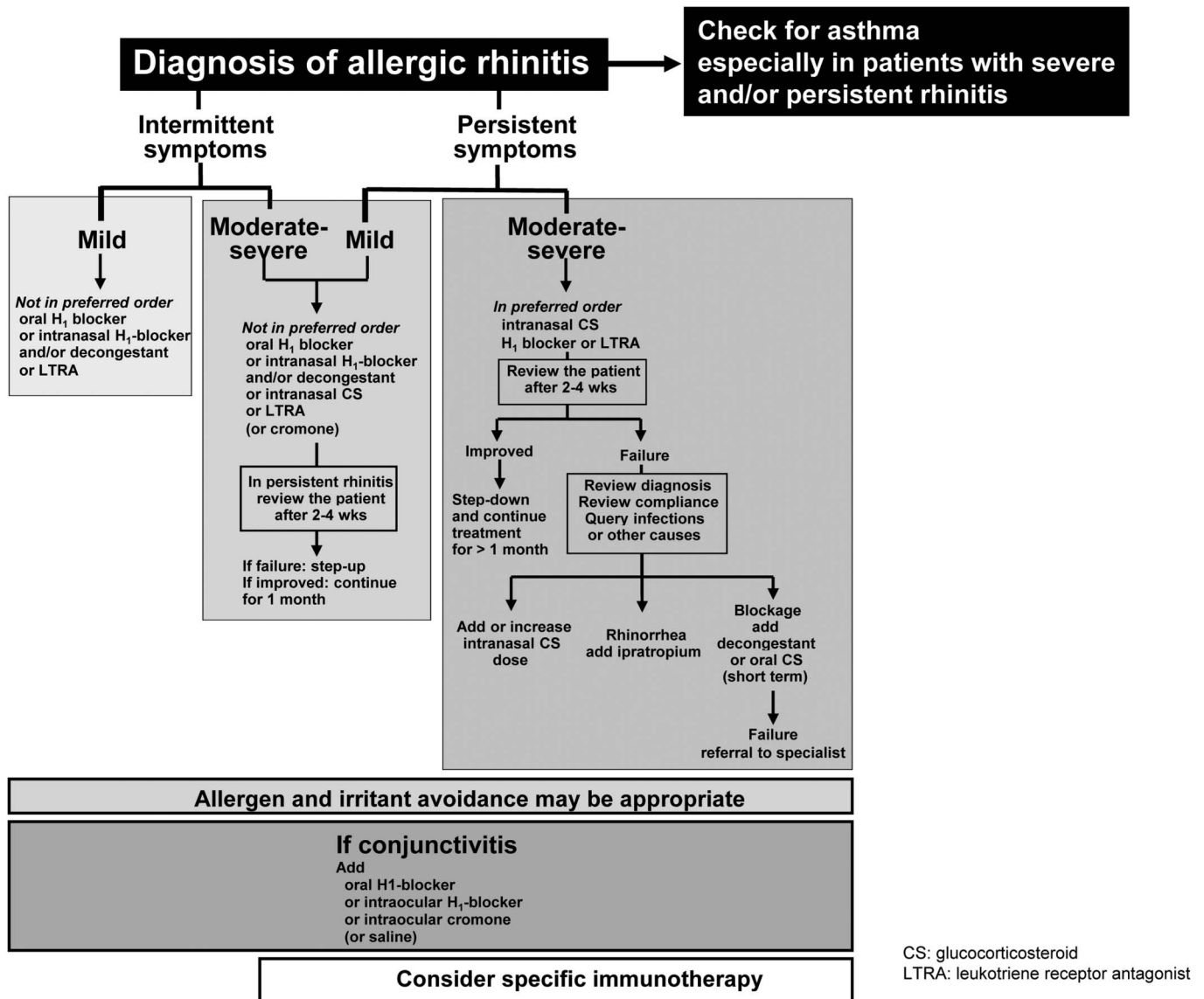


FIGURE 1. An algorithm of the management of Allergic Rhinitis ARIA update 2008.

almost 50%.<sup>79</sup> Allergen-specific immuno-therapy in patients with AR has a prolonged preventive effect on the development of asthma when stopped.<sup>76</sup>

## ASTHMA AND ALLERGIC RHINITIS IN ASIA PACIFIC

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 middle-income countries.<sup>80,81</sup> In Thailand, the prevalence of all 3 major allergic diseases increased significantly from the ISAAC phase I survey performed in 1995; that is, asthma increased from 12.2% to 14.5%, AR from 37.9% to 50.6%, and eczema from 9.8% to 15.7%. In Japan, rhinitis has increased from 3.8% in 1982 to 32% and asthma from 4.6% in 1992<sup>82</sup> 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,<sup>83</sup> and more recently, the overall cumulative and 12-month prevalence of wheezing and rhinitis in younger children 10 to 12 years was 8.2% and 44.4%, respectively; and in the older children 13 to 15 years, 6.9% and 42.2%.<sup>84</sup> Similarly, in Singaporean preschoolers, the cumulative and previous 12-month 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.<sup>85</sup> Although asthma prevalence in rural Bangladesh is 16.1%<sup>86</sup> and in Pakistan there is a doubling of the prevalence of AR and asthma in ISAAC III as compared with ISAAC I, in a study in urban India the overall prevalence of asthma was 2.38%.<sup>87</sup> Prevalence of allergic rhinitis in 5- to 11-year-old children in Vietnam is 34.9%<sup>88</sup> and prevalence of allergic rhinitis in patients with asthma is 48.54% (Le Van Khang et al. Study of sensitivity, specificity of house dust mite allergen made in Vietnam in diagnosis of asthma. Ministry of Health of Vietnam, January 2002 to December 2004, www.cimsi.org.vn). Asthma prevalence in Australia increased from 8% in 1989–1990 to 11% in 1995 but the prevalence plateaued in recent years with a 2004 prevalence of asthma at 14% to 16% of children and 10% to 12% of adults.<sup>89</sup>

Although overall regional data for adults is scant, it is estimated that 1% to 10% have asthma and 10% to 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.<sup>90</sup> More recent data showed an increase in prevalence of AR in Korea from 6% to 10%<sup>90</sup> to >20%<sup>91</sup> 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%).<sup>92</sup>

### Comorbid Allergic Rhinitis and Asthma

Recent data showed a very high comorbid rate of asthma and rhinitis as 60% to 80% of patients with asthma had rhinitis symptoms.<sup>93</sup> The younger patients with asthma had a higher comorbid rate of rhinitis (80%) than elderly

patients (60%); furthermore, patients with asthma who also had rhinitis presented more severe clinical symptoms in both adults and children, indicating that rhinitis may affect asthma severity and outcome.<sup>93</sup>

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.<sup>94</sup>

### Impact on Quality of Life

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.<sup>95</sup> Twenty-seven percent of adults and 37% of children with asthma reported absences from work or school in the previous year because of asthma, and 40% required hospitalization, emergency department visits, or unscheduled emergency visits to other health care facilities in the previous year.<sup>95</sup> 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 4 Asian countries, most children with asthma (73%) had pre-existing symptoms of AR and asthma with comorbid AR substantially affecting their quality of life and worsening their asthma symptoms.<sup>5</sup> However, awareness of the comorbidity of AR and asthma among the parents of children with asthma was only about 50%.

From the evidence listed in this summary, it is clear that there is a high linkage between asthma and AR in the Asia Pacific too. 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. However, 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 speciality in some countries and 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.

On the basis of 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.

## CONCLUSIONS

The prevalence of asthma and AR is increasing in Asia Pacific and the prevalence of comorbidity is high.<sup>96</sup> The perception of patients and physicians regarding the links between asthma and rhinitis varies between countries, but seems to be higher than expected.<sup>77,78</sup> However, knowledge is not directly translated into practice because fewer physicians coprescribe treatments for rhinitis and asthma in the same patient.

The recommendations of the ARIA workshop in 1999 are still valid,<sup>15</sup> 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.

#### ACKNOWLEDGMENT

This article is based on the presentation given at the BANYU Symposium at the 20th World Allergy Congress in Bangkok in December 2007.

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