Prevention of Allergy and Allergic Asthma
Chemical Immunology and Allergy
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Introduction

The prevalence of asthma and allergy is increasing. It is estimated that over 20% of the world’s population suffer from IgE-mediated allergic diseases such as asthma, rhinoconjunctivitis, eczema and anaphylaxis. Asthma, which in more than 50% of adults and 70–80% of children is allergic, occurs in around 5–15% in the paediatric population. Asthma is estimated by the World Health Organization (WHO) to affect 150 million people worldwide, placing an enormous strain on health resources in many countries, and is a major cause of hospitalisations for chronic diseases in children in the Western World.

Prevention of Allergy and Allergic Asthma was a collaborative project between the World Allergy Organization (WAO) and the WHO. This collaboration was commissioned to advance the strategic objectives of the WHO as outlined in its Strategy for the Prevention and Control of Chronic Respiratory Diseases.

WAO and WHO created a working group consisting of seven ‘Chapter Chairpersons’, each with co-authors, and a meeting of the group took place on December 5–6, 1999, at the WHO headquarters in Geneva. The Chairpersons of the working group invited a number of international experts to contribute to the chapters, enabling WAO and WHO to benefit from the widest possible expert opinion in the development of this document. A report of the second meeting of the working group was published in September 2003 [1].

The strategic guidelines and recommendations in this document have been developed for use by governments, health care professionals, research grant providers, lay organizations, and patients, and will be disseminated, amongst other routes, through the WAO educational program, Global Resources in Allergy.
What this Document Provides

The document provides guidelines and recommendations for the prevention of the allergen-specific immunological sensitisation necessary for disease, and advises that even where it exists, this sensitisation is not always expressed as disease. Allergic diseases can involve the respiratory system, e.g. asthma and rhinitis, the gastro-intestinal tract, e.g. food allergy, or the skin, e.g. eczema and contact dermatitis. In rare cases a generalised reaction, allergic anaphylaxis, develops, which can lead to shock and death. A source of potential confusion is that each allergic disease has a clinical mirror image, based on similar inflammatory reactions, but which is not initiated or mediated by specific immunological reactions.

In the westernised world, allergy and asthma have increased two- to three-fold over the last 40 years and have reached epidemic proportions. The increase in these diseases has occurred over a period of persistent environmental and lifestyle changes. Epidemiological studies have shown great variation in the prevalence of asthma and allergies between different nations. Valuable information may be derived from areas where a rapid increase in disease has occurred, to form the basis for prevention strategies in areas where the prevalence of these diseases is still low.

Most of the data on which the guidelines are based have been obtained from countries that have experienced this rapid increase in allergies and asthma, and so will require interpretation and adaptation to meet different local circumstances. Within any country or region, climatic and environmental variations, and differences between affluent and non-affluent groups, may require a broad range of strategies and advice to be available. It is hoped that the general principles of prevention proposed in this document will provide a useful basis for local guidelines to be developed. Further research is essential on many aspects which are still not fully understood, and further actions are recommended in each section to assist the strategic development of national and international research programmes.

Primary prevention (see Glossary on page XVII) of asthma may often be secondary prevention of allergy.

This document focuses mainly on primary prevention of the allergen-specific immunological sensitisation that is the basis for allergy and for much of asthma. Primary prevention measures should be implemented if they meet the following criteria:

They should be of potential benefit to the major part of the population.
They should be of no known harm to anyone.
They should not involve unreasonable costs.

Secondary prevention is also covered in some detail since adequate diagnosis and treatment of allergic diseases such as eczema and allergic rhinitis at a young age can prevent the later development of asthma.
Tertiary prevention is briefly mentioned; it is covered in detail elsewhere, for example in the Global Resources in Allergy program of the WAO, the ‘Global Initiative for Asthma’ [2], and ‘Allergic Rhinitis and Its Impact on Asthma’ [3]. The models of occupational respiratory and skin allergies are introduced as examples where primary and secondary prevention strategies have been successful.

Non-allergic asthma is mentioned in this report since some secondary prevention strategies may be of value in this disorder. Although the causes are less well defined, similar inflammation is present in the airways of patients with non-allergic asthma as in allergic asthmatics.

**Evidence Base**

In creating this document, authors were asked to code the referenced documents in accordance with the following WHO Categories of Evidence; on the basis of the categorisation of evidence, a strength of recommendation may be awarded to the ensuing guidelines. The Categories of Evidence are more easily applied to therapeutic interventions than to epidemiological and basic research studies, where randomisation or blinding may not be possible. A well-designed physiological study, for example, may not be able to be coded by these criteria. Thus, a recommendation awarded a ‘b’ cannot always be interpreted as a lesser recommendation than one coded ‘a’ – it is an indication only of the type of studies which have created the evidence base: a recommendation awarded ‘d’ may indicate that at the present time there is an absence of evidence. Accordingly, it was decided only to restrict strength of recommendation categories to the guidelines in chapters 5 and 6, where a clear interpretation of the evidence base is possible.

**WHO Categories of Evidence**

Ia: Evidence from meta-analysis of randomised controlled trials  
Ib: Evidence from at least one randomised controlled trial  
IIa: Evidence from at least one controlled study without randomisation  
IIb: Evidence from at least one other type of quasi-experimental study  
III: Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies  
IV. Expert opinion of the Prevention of Allergy and Allergic Asthma working group
**WHO Strength of Recommendations:**

A: Directly based on category I evidence  
B: Directly based on category II evidence or extrapolated recommendation from category I evidence  
C: Directly based on category III evidence or extrapolated recommendation from category I or II evidence  
D: Directly based on category IV evidence or extrapolated recommendation from category I, II or III evidence

**Glossary and Definitions**

The nomenclature of allergy is varied, and to address this important topic and ensure clear communication between health professionals, the WAO recommends the adoption of a global nomenclature for allergy. The terminology proposed by the European Academy of Allergology and Clinical Immunology publication, ‘A Revised Nomenclature for Allergy’ [4] has been updated by the WAO in its publication ‘A Revised Nomenclature for Allergy for Global Use’ [5]. The WAO nomenclature is used throughout this document.

**Allergy.** Allergy is a hypersensitivity reaction initiated by immunological mechanisms. Allergy can be antibody or cell mediated. In the majority of cases the antibody typically responsible for an allergic reaction belongs to the IgE isotype, and these individuals may be referred to as suffering from an IgE-mediated allergy. Not all IgE-associated ‘allergic’ reactions occur in ‘atopic’ subjects. In non-IgE-mediated allergy the antibody can belong to the IgG isotype, e.g. anaphylaxis due to immune complexes containing dextran, and the classical, nowadays rare, serum sickness previously referred to as a type III reaction. Both IgE and IgG antibodies are found in allergic bronchial pulmonary aspergillosis. Allergic contact dermatitis is representative of allergic diseases mediated by lymphocytes.

**Allergens.** Allergens are antigens which cause allergy. Most allergens reacting with IgE and IgG antibody are proteins, often with carbohydrate side chains, but in certain circumstances pure carbohydrates have been postulated to be allergens. In rare instances low-molecular-weight chemicals, e.g. isocyanates and anhydrides acting as haptens, are still referred to as allergens for IgE antibodies. In the case of allergic contact dermatitis, the classical allergens are low-molecular-weight chemicals, e.g. chromium, nickel and formaldehyde, reacting with T cells.

**Atopy.** Atopy is a personal and/or familial tendency, usually in childhood or adolescence, to become sensitised and produce IgE antibodies in response to
ordinary exposure to allergens, usually proteins. As a consequence, such indi-
viduals can develop typical symptoms of asthma, rhinoconjunctivitis, or
eczema. The terms ‘atopy’ and ‘atopic’ should be reserved to describe the
genetic predisposition to become IgE sensitised to allergens commonly occur-
rating in the environment and to which everyone is exposed but to which the
majority do not produce a prolonged IgE antibody response. Thus, atopy is a
clinical definition of an IgE antibody high-responder. The term atopy cannot be
used until an IgE sensitisation has been documented by IgE antibodies in serum
or by a positive skin prick test. Allergic symptoms in a typical atopic individ-
ual can be referred to as atopic, e.g. atopic asthma. However IgE-mediated
asthma in general should not be called atopic asthma. Neither a positive skin
prick test nor presence of IgE antibody to a less common allergen, e.g.
Hymenoptera sting or a drug, which are high-dose exposures, is a diagnostic
criterion for atopy.

*Hypersensitivity*. Hypersensitivity causes objectively reproducible symp-
toms or signs, initiated by exposure to a defined stimulus that is tolerated by
normal subjects.

*Non-Allergic Hypersensitivity*. Non-allergic hypersensitivity is the pre-
ferred term to describe hypersensitivity in which an immunological mechanism
cannot be proven.

*Prevention*

Primary Prevention: Prevention of immunological sensitisation (i.e. the
development of IgE antibodies).

Secondary Prevention: Preventing the development of an allergic disease
following sensitisation (and the progression from eczema or rhinoconjunctivi-
tis into severe diseases such as asthma).

Tertiary Prevention: Treatment of asthma and allergic diseases.

*Disease Nomenclature*

*Asthma* (as defined by the Global Initiative for Asthma). Asthma is a
chronic inflammatory disorder of the airways in which many cells play a role,
in particular mast cells, eosinophils and T lymphocytes. In susceptible individ-
uals this inflammation causes recurrent episodes of wheezing, breathlessness,
chest tightness, and cough particularly at night and/or in the early morning.
These symptoms are usually associated with widespread but variable airflow
limitation that is at least partly reversible either spontaneously or with treat-
ment. This inflammation also causes an associated increase in airway responsiv-
ess to a variety of stimuli.

*Occupational Asthma*. It is characterised by variable airflow limitation
and/or airway hyperresponsiveness due to causes and conditions attributable to
a particular occupational environment and not to stimuli encountered outside the workplace.

**Allergic Asthma.** It is the basic term for asthma mediated by immunological mechanisms. When there is evidence of IgE-mediated mechanisms the term IgE-mediated asthma is recommended. IgE antibodies can initiate both an immediate and a late asthmatic reaction. However, as in other allergic disorders, T-cell-associated reactions seem to be of importance in the late and delayed reactions. Depending on the duration of symptoms, asthma can be referred to as either intermittent or persistent (as recommended in the document ‘Allergic Rhinitis and Its Impact on Asthma’ [3]).

**Non-Allergic Asthma.** This is the preferred term for non-immunological types of asthma. It is recommended that the old terminologies, ‘extrinsic’, ‘intrinsic’, ‘exogenous’ and ‘endogenous’ should no longer be used to differentiate between the allergic and non-allergic sub-groups of asthma.

**Rhinoconjunctivitis.** Symptoms of an immunologically mediated hypersensitivity reaction in the nose and conjunctiva should be referred to as allergic rhinoconjunctivitis. Most cases are IgE mediated. Based on the duration of symptoms, it can be useful to differentiate between intermittent and persistent allergic rhinoconjunctivitis.

**Dermatitis.** The umbrella term for a local inflammation of the skin should be dermatitis. What is generally known as ‘atopic eczema/dermatitis’ is not one, single disease but rather an aggregation of several diseases with certain characteristics in common. A more appropriate term is eczema. The subgroup related to allergic asthma and rhinoconjunctivitis, i.e. eczema in a person of atopic constitution, should be called atopic eczema.

Close contact with low-molecular-weight chemicals may provoke a predominantly Th1-lymphocyte-mediated allergic contact dermatitis. The non-allergic variety can also be described by terms like irritant/toxic contact dermatitis.

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