Prevention of Allergy and Allergic Asthma
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World Allergy Organization Project Report and Guidelines

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Chemical Immunology and Allergy

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Contents

XIII Introduction
  S.G.O. Johansson, Sweden; Tari Haahtela, Finland

XIV What this Document Provides

XV Evidence Base

XV WHO Categories of Evidence

XVI WHO Strength of Recommendations

XVI Glossary and Definitions

XVI Allergy

XVI Allergens

XVI Atopy

XVII Hypersensitivity

XVII Non-Allergic Hypersensitivity

XVII Prevention

XVII Disease Nomenclature

XVII Occupational Asthma

XVIII Allergic Asthma

XVIII Non-Allergic Asthma

XVIII Rhinoconjunctivitis

XVIII Dermatitis

XVIII References

1 Genetics
  J.W. Holloway, S.T. Holgate, United Kingdom

  1 The Heritability of Atopic Disease
  2 Is Atopy a Heritable Condition?
  6 Molecular Regulation of Atopy and Atopic Disease
Susceptibility Genes
Approaches to Genetic Studies of Complex Genetic Diseases
Genome-Wide Screens
Novel Asthma Susceptibility Genes Identified through Genome Scans
Candidate Regions
Chromosome 11q13
Chromosome 5q31–35
IL-4 and the IL-4 Receptor
Interleukin-13
β2-Adrenergic Receptor
CD14
SPINK5/LEKTI
Chromosome 12
Human Leukocyte Antigen and T-Cell Receptor-α/β
Disease-Modifying Genes
Genetic Influences on Disease Severity
Genetic Regulation of Response to Therapy – Pharmacogenomics
Conclusions
The Future
References

Environmental Influences on Asthma and Allergy
M.I. Asher, New Zealand; E. Dagli, Turkey

Background
Evolution in the Understanding of the Relationship between Environmental Factors and Allergic Disease
Research Approaches
The Diseases
Preventive Strategies
Major Changes in Population Prevalence Suggesting Environmental Influences

Diet
Fish
Vegetables, Fruit and Antioxidants
Cereals and Rice
Polyunsaturated Fat
Trans Fatty Acids
Chemicals and Trace Elements
Sodium
Selenium
Magnesium
Food Preservatives and Additives
Breast-Feeding
Maternal Diet during Lactation
Maternal Diet in Pregnancy
Growth
55  Low Birth Weight
55  Disproportionate Foetal Growth
56  Obesity
56  Physical Fitness
57  Infection
58  General Burden of Childhood Infections
58  Day Care
59  Family Size and Sibling Order
59  Specific Infections
59  Respiratory Syncytial Virus
59  Tuberculosis
60  Measles Infection
60  Orofaecal Infections
61  Pertussis
61  Anthroposophical Lifestyle
61  Immunisation
63  Microbial Exposure in Early Life
63  Intestinal Microflora Protective
63  Probiotics
64  Antibiotics
66  Farming Environment
67  Endotoxin
69  Airborne Allergens
69  Allergens
69  The Allergens
70  Risk of IgE Sensitisation
71  Allergen Avoidance and Prevention
74  Methods for Allergen Avoidance
75  Indoor Environment
75  Environmental Tobacco Smoke
75  Tobacco Exposure
75  Effect of Active Smoking on the Airways
76  Mechanisms of Action of Environmental Tobacco Smoke
76  Clinical Evidence
77  Prenatal Exposure
78  Postnatal Exposure
80  Damp and Mould
81  Cooking Gas and Nitrogen Dioxide
82  Indoor Heating
82  Formaldehyde and Other Volatile Organic Compounds
82  Other Features of Homes
82  Pillows
83  Outdoor Air Pollution
85  Other Population Factors
85  Economic Factors
85  Water Supply

Contents
Contents

86 Climate
87 Conclusion
88 Acknowledgement
88 References

102 Early Immunological Influences
   P. Holt, Australia; C. Naspitz, Brazil; J.O. Warner, United Kingdom

104 Ontogeny of Allergic Responses in the Antenatal Period
108 Fetal Nutrition
109 Lung Growth and Development
109 T-Cell Responses to Allergens during Infancy and Early Childhood
112 Allergen-Specific T-Cell Immunity and Expression of Allergic Disease
113 Environmental Factors and Allergy/Asthma
115 Prevention of the Development of Persistent Allergic Disease
115 Potential Options for Intervention in Early Childhood
117 Non-Specific Immunostimulation during Infancy
117 Immunoprophylaxis
118 Allergen Avoidance
118 Pollutants
119 Early Therapeutic Interventions
120 New-Generation ‘Th2-Antagonistic’ Drugs
120 Use of Anti-Virals in Childhood
120 Conclusions
121 References

128 Prediction and Early Diagnosis
   U. Wahn, Germany; A. Chuchalin, Russia; M.L. Kowalski, Poland

128 Prediction at Birth
129 Family History
129 Genetic Markers
131 Immunological Markers
132 Prediction at an Early Stage of the Disease Process
132 Conclusions
133 References

135 Preventive Measures: Section 1: Early Interventions
   A. Høst, Denmark; A. Boner, Italy; J. Odhiambo, Kenya
   Contributors: A. Custovic, United Kingdom; R. Lockey, USA

135 Possible Strategies in Individuals at High Risk and in the General Population
136 Methodology in Preventive Studies
136 Infants without a Special Risk for Allergic Disease
137 Infants with a High Risk of Allergic Disease
139 Children with Allergic Symptoms (Secondary and Tertiary Prevention)
139 Specific Treatment
139 Avoidance

Acknowledgement

References
Allergy Vaccination
Pharmacological Intervention in Infants/Children with Atopic Eczema
Other Measures (Avoidance of Irritants, Especially Tobacco Smoke)
Corticosteroids and Cromones
Leukotriene Antagonists
Theophyllines
New Generation ‘Th2-Antagonistic’ Drugs
Implementation of Preventive Measures
Primary Prevention: Evidence-Based Recommendations
Secondary Prevention: Evidence-Based Recommendations
Tertiary Prevention: Evidence-Based Recommendations
Rhinitis, Rhinosinusitis
Aspirin Triad
Gastro-Oesophageal Reflux Disease
Further Research Recommendations
References

Preventive Measures: Section 2: Occupational Allergies and Asthma
K. Venables, United Kingdom; J. Ring, Germany; J. Sastre, Spain

Occupational Asthma
Exacerbation of Existing Asthma
Heavy Exposures and Irritant-Induced Asthma
Pharmacologically Active Agents
Sensitisation
Morbidity and Co-Morbidities
Induction and Provocation of Asthma
Prevention of Sensitiser-Induced Asthma
Secondary Prevention
Tertiary Prevention
Occupational Skin Diseases
Natural Rubber Latex Allergy
Recommendations
Occupational References

Allergy and Asthma Education
B. Volovitz, Israel; P. Vichyanond, Thailand; N.-S. Zhong, China
Contributors: J. Ring, Germany; M. Hemmo-Lotem, Israel; G. Walter Canonica, Italy;
R. Lockey, USA; C.E. Baena-Cagnani, Argentina; T. Schäfer, Germany

Asthma Education
Asthma Education in Children
Burden of Asthma in Childhood
Why Is Asthma Underdiagnosed and Undertreated in Childhood?
Effectiveness of Patient Education Programmes for Children
Importance of the Physician-Patient Partnership

Contents IX
Cost-Effectiveness of Asthma Education
Contents of an Educational Programme
Example of an Asthma Education Programme
Basic Facts about Asthma
Change of Negative Attitudes
Improvement in Management Skills
Preventive Measures
Recognition of the Early Signs of an Attack
Rhinitis Education
Contents of an Allergic Rhinitis Education Programme
Basic Information on How Allergic Rhinitis Develops
Appropriate Avoidance Measures
Medications
Non-Pharmacologic Therapy
Related Conditions
Education in Eczema
Burden and Triggers of Eczema
Education and Prevention Programmes
Example of an Eczema Education Programme
Allergic Contact Dermatitis
Severe Reactions, Allergic Anaphylaxis
International Coalition for Allergy and Asthma Prevention
References

The Costs of Allergy and Asthma and the Potential Benefit of Prevention Strategies
K. Weiss, USA; M. Haus, South Africa; Y. Iikura, Japan
Contributor: A. Kaplan, USA

The Costs of Illness
Building Strategies for a Health Economic Benefit of Prevention of Asthma and Allergies
Policy Implications for Programmes Targeting at the Prevention of Allergy and Asthma
Conclusions
Recommendations
References

Summary and Guidelines
S.G.O. Johansson, Sweden; T. Haahtela, Finland

Genetics
Current Knowledge
Further Actions Required
Environmental Influences
Current Knowledge
Further Actions Required

Contents X
Contents

195 Early Immunological Influences
195 Current Knowledge
195 Further Actions Required
195 Predictive and Early Diagnosis
195 Current Knowledge
196 Further Actions Required
196 Preventive measures
196 Guidelines
196 Primary Prevention
197 Secondary Prevention
197 Tertiary Prevention
197 Further Actions Required
198 Further Actions for Occupational Allergies
198 Education
198 Guidelines
198 Further Actions Required
199 Costs of Allergies and Asthma
199 Guideline
199 Further Actions Required

200 Appendix 1: Patient Information Sheets: Pull-Out Sheets of Practical Allergen Avoidance Advice
200 House Dust Mite Allergen Reduction
201 Pollen Avoidance
201 Pet Allergen Avoidance
202 Cockroach Allergen Avoidance
202 Mould Allergen Avoidance
203 Severe Reactions, Allergic Anaphylaxis

204 Appendix 2: Content of Educational Programs in Allergy and Allergic Asthma
204 Allergic Asthma and Allergic Rhinitis
204 Eczema
205 Severe Reactions, Allergic Anaphylaxis

206 Author Index

207 Subject Index
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 gastrointestinal 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 individuals 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 occurring 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 individual 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 symptoms or signs, initiated by exposure to a defined stimulus that is tolerated by normal subjects.

**Non-Allergic Hypersensitivity.** Non-allergic hypersensitivity is the preferred 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 rhinoconjunctivitis 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 individuals 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 treatment. This inflammation also causes an associated increase in airway responsiveness 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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References


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