WAO
White Book on Allergy
EXECUTIVE SUMMARY
Update 2013
WAO White Book on Allergy: Update 2013

Executive Summary

Ruby Pawankar
Giorgio Walter Canonica
Stephen T. Holgate
Richard F. Lockey
Michael S. Blaiss
WAO White Book on Allergy: Update 2013, Executive Summary

Editors

Prof. Ruby Pawankar, MD, PhD
WAO President
Professor of Allergy
Department of Pediatrics
Nippon Medical School
1-1-5, Sendagi
Bunkyo-ku,
Tokyo 113-8603
JAPAN
pawankar.ruby@gmail.com

Prof. Stephen T. Holgate, BSc, MD, DSc, FMed Sci
WAO Treasurer
Medical Research Council Clinical Professor of Immunopharmacology
Infection, Inflammation and Immunity
School of Medicine
University of Southampton
Level F, South Block
Southampton General Hospital
Tremont Road
Southampton SO16 6YD
United Kingdom

Prof. Giorgio Walter Canonica, MD
WAO, Historian
Allergy & Respiratory Diseases
Department of Internal Medicine
University of Genoa
IRCCS AOU S.Martino, Largo Rosanna Benzi
101-16132 Genoa
ITALY

Prof. Richard F. Lockey, MD
WAO Past President
Division of Allergy & Immunology
Joy McCann Culverhouse Chair in Allergy & Immunology
University of South Florida College of Medicine
James Haley Veterans Administration Medical Center (111D)
13000 Bruce B. Downs Boulevard
Tampa, Florida 33612
USA

Prof. Michael S. Blaiss, MD
WAO Board Member
Clinical Professor of Pediatrics and Medicine
University of Tennessee Health Science Center
7205 Wolf River Blvd
Germantown, Tennessee 38138
USA

ISBN-10: 0615929176 (print)
ISBN-10: 0615929184 (digital)

Copyright 2013 World Allergy Organization (WAO). All rights reserved.
No part of this publication may be reproduced in any form without the written consent of the World Allergy Organization.
This book is not for sale.

World Allergy Organization
555 East Wells Street
Suite 1100
Milwaukee, Wisconsin 53202
United States of America
Phone: +1 414 276 1791
Fax: +1 414 276 3349
Email: info@worldallergy.org
Website: www.worldallergy.org

Printed in the United States, 2013
Introduction to the Executive Summary

Allergic Diseases as a Global Public Health Issue
R Pawankar, GW Canonica, ST Holgate, RF Lockey, MS Blaiss

Introduction

The prevalence of allergic diseases worldwide is rising dramatically in both developed and developing countries. These diseases include asthma; rhinitis; anaphylaxis; drug, food, and insect allergy; eczema; and urticaria (hives) and angioedema. This increase is especially problematic in children, who are bearing the greatest burden of the rising trend which has occurred over the last two decades. In spite of this increase, even in the developed world, the care of patients with allergic diseases is fragmented and far from ideal.

One other important aspect we highlight is the need for better adherence to treatment. In light of the observations that adherence to treatment in Chronic Diseases is less than 50% and the cost of non-adherence highly impacts the burden of chronic diseases worldwide, adherence needs to be a priority patient-related outcome and an important step in patient education.

Allergy not only causes long-term immune dysfunction, but also has underlying inflammation, which forms the underlying factor for other non-communicable diseases. Another important factor that comes into play are the gene-environment interactions. Because of the huge extent of allergy prevalence, allergy should be regarded as a major public health problem and within the framework of non-communicable diseases.

Finally, the declaration of the WAO recommends to conduct more epidemiological studies to establish the true burden of allergic diseases and asthma, initiate more allergens and environmental control measures, enhance levels of research and clinical practice available across different countries, provide undergraduate and post-graduate education and training and recognize the specialty of allergy and increase public awareness of allergic diseases and their prevention to decrease the burden of allergic diseases globally in future years. A concerted effort of multiple stakeholders is essential to address this issue. The World Allergy Organization is greatly concerned about the increasing global burden of allergic diseases and is committed to increased collaboration and communication at a global level, engaging governments and policy makers to channel resources and efforts to recognize allergic disease as a public health issue. In light of this, the World Allergy Organization developed the original WAO White Book on Allergy published in 2011. As there are new data, new evidences and new treatments, WAO considers it is timely to update several chapters.

The WAO White Book on Allergy: Update 2013 has provided not only our member societies but also national health ministries, governments, patient groups, and other medical societies around the world with a definitive resource of information on the various aspects of asthma and allergic diseases especially that pertain to their area. The data from national member societies reinforce the book’s central purpose to be an advocacy tool to show the increasing prevalence of asthma and allergic disease worldwide, especially in children, and the subsequent growing burden carried by all, and the absolute necessity of increased service provision. Therefore, it is imperative for this content to remain up-to-date as an authoritative global resource.

The WAO White Book on Allergy: 2013 Update has accomplished just that! We have taken the core document of the original WAO White Book on Allergy and updated it to contain new information to existing information and provided you with the latest data and evidences on allergies as a global public health issue.

1. THE BURDEN OF ALLERGIC DISEASE

Allergic Rhinitis

- Allergic rhinitis (AR) results from an IgE-mediated inflammation of the nasal mucosa.
- The disease currently affects between 10% and 30% of the population.
- Studies indicate that prevalence rates are increasing worldwide.
- The classification proposed in the Allergic Rhinitis and its Impact on Asthma (ARIA) guidelines is useful for the implementation of treatment.
- AR is a risk factor for asthma.
- Other co-morbidities of AR include: sinusitis, nasal polyposis, conjunctivitis, otitis media with effusion, upper respiratory infections, breathing through the mouth, and sleep disorders.
- AR has a significant impact on patients based on the degree of the severity of their symptoms. It has psychological effects, interferes with social interactions, and creates an economic burden not only for the affected subject, but for the family and for the society at large.
- Management is based on patient education, environmental control measures, pharmacotherapy and specific immunotherapy.
**Allergic Conjunctivitis**
- Allergic conjunctivitis is an increasingly prevalent allergic disease, with the same clinical gravity as allergic asthma and allergic rhinitis.
- The umbrella term “allergic conjunctivitis” includes distinct clinical entities, from mild but disturbing forms due to IgE sensitization to aeroallergens; to forms of keratoconjunctivitis where the severe allergic inflammation, with corneal involvement, is more difficult to diagnose and treat, and may lead to permanent ocular damage and even loss of vision.

**Rhininosinusitis**
- Rhinosinusitis (RS) is one of the most common and expensive medical conditions.
- RS occurs in a number of forms, the most common of which are either acute or chronic.
- Initial treatment of RS is usually by a primary care physician (PCP) and if unsuccessful, the PCP should refer either to a surgeon or to an allergist for specialized care.
- In the vast majority of cases, RS is controlled by proper medical management without the need for surgery.
- Surgery should only be considered in those patients who are properly managed but in whom a number of medical treatment programs fail.
- The Allergist, who is trained in allergy, immunology, microbiology, internal medicine and/or pediatrics combined with an expert knowledge of nasal and sinus anatomy and appropriate pharmacology, is best suited to manage RS.

**Asthma**
- Asthma is a life-long chronic inflammatory disorder of the airways, associated with variable structural changes, that affects children and adults of all ages. It is associated with airway hyperresponsiveness and airflow obstruction that is often reversible either spontaneously or with treatment.
- When uncontrolled, asthma can cause death, and can markedly interfere with normal activities, seriously impacting an individual’s quality of life.
- Because of under-diagnosis and inadequate treatment, asthma presents a serious public health problem throughout the world; especially in low and middle income countries.
- Atopy - the genetic predisposition to develop IgE-mediated sensitivity to common aeroallergens, is the strongest identifiable predisposing factor to the development of asthma, especially in children.
- There was a sharp increase in the prevalence, morbidity, and mortality associated with asthma beginning in the 1960s and 1970s in the so-called “Westernized” countries of the world.
- The prevalence of asthma in different countries varies widely, but the disparity is narrowing due to rising prevalence in low and middle income countries as they adopt a more Western-type lifestyle. It is plateauing in high income countries.
- Inhaled corticosteroids are currently the most effective anti-inflammatory medications to treat persistent asthma.
- The monetary costs of asthma are substantial and include both direct medical costs and the indirect costs, the latter associated with time lost from work and premature deaths.
- National efforts to tackle asthma as a public health problem, such as the program introduced in Finland and Ireland, produce remarkable benefits that are reflected in dramatic reductions in deaths and hospital admissions.
- Many barriers exist to a reduction in the worldwide burden of asthma.
- There are unmet diagnostic, therapeutic, educational and financial needs to achieve better worldwide control of asthma.
- More effort is needed to concentrate on ways to improve the management of asthma by focusing on disease control both in primary and secondary care rather than treating acute episodes. This concept has to be embedded in healthcare programs

**Severe Asthma**
- Severe asthma is defined as asthma which requires treatment with high dose inhaled corticosteroids plus a second controller and/or systemic corticosteroids, to prevent it from becoming “uncontrolled” or which remains “uncontrolled” despite this therapy.
- Patients presenting with persistent symptoms despite high dose asthma therapy should be systematically evaluated to confirm the diagnosis of asthma, adherence with treatment and to identify manage any underlying co-morbidities or aggravating factors.
- Severe refractory asthma constitutes only a small subset of all patients with uncontrolled asthma and is phenotypically heterogeneous at clinical and molecular levels.
- The burden of severe asthma is substantial with high per-person annual costs which can be largely attributed to medications, hospital admissions, and work loss.
• Current therapeutic options are limited in severe asthma but novel biologic therapies targeting Th2 inflammation will soon be available and will require a phenotype specific approach to treatment.
• Future work will focus on understanding and developing new therapeutic targets for ‘non-Th2’ mechanisms in severe asthma.

Atopic Eczema
• An increase in the worldwide prevalence of atopic eczema has been observed.
• Atopic eczema is the most common chronic inflammatory skin disease with a varied clinical spectrum.
• Atopic eczema is often the first manifestation of the atopic patient and early intervention may offer an opportunity to impede or stop the atopic march.
• Atopic eczema represents an important public health issue due to its impact on quality of life and its socio-economic burden.

Anaphylaxis
• Epinephrine (adrenaline) at appropriate doses, injected intramuscularly into the mid-anterior lateral thigh, is the drug of choice to treat anaphylaxis.
• There is lack of consensus about the definition and diagnostic features of anaphylaxis and this definition contributes to the variability in its identification, treatment and the use of epinephrine.
• The variability and severity of anaphylaxis is somewhat dependent on the route by which the allergen or inciting agent is delivered, e.g., parenteral versus oral administration; the former is commonly associated with more severe reactions.
• There are a variety of other terms which describe anaphylaxis and which cause confusion, especially with its definition and treatment. These include: generalized systemic reaction; systemic allergic reaction; constitutional reaction; and serious hypersensitivity reaction.
• The illustrations in the World Allergy Organization Guidelines for the Assessment and Management of Anaphylaxis, published in 2011 and updated in 2012, are ideal for all physicians and other healthcare professionals.1,2
• Anaphylaxis includes both allergic and non-allergic etiologies.
• The term “anaphylactoid” is outdated.

Food Allergy
• Globally, 240 – 550 million people may suffer from food allergy.
• Food allergy significantly affects the quality of life of sufferers (mainly children).
• Stakeholders must be prepared to meet the needs of patients by enhancing the diagnostic process, the traceability of responsible foods, and the availability of substitute foods, assisting hospitalized patients, and preventing mortality.
• Large areas in the world lack legislation on food labeling.
• As diagnostic and therapeutic decision strategies are not clear-cut, evidence-based guidelines are necessary for clinicians, patients, governments and industry to deal with the challenge of food allergy. Such guidelines, eg, the WAO recommendation on the Diagnosis and Rationale Against Cow’s Milk Allergy (DRACMA) are available and are ready to be implemented.
• Epidemiologic studies are necessary, in particular, in less developed areas of the world.
• Oral desensitization represents a promising approach to reduce the burden of disease caused by food allergy.

Urticaria and Angioedema
• Urticaria is a heterogeneous group of disease sub-types characterised by wheals, angioedema or both.
• Three major categories exist: a) spontaneous occurrence of wheals, associated with acute and chronic urticaria; b) wheals and angioedema elicited by specific stimuli, and in particular physical urticarias; and c) other urticarial disorders such as exercise-induced urticaria.
• Urticaria occurs frequently, with a lifetime prevalence above 20%.
• Except for acute urticaria, diagnostic and therapeutic procedures can be complex and referral to a specialist is often required.
• Untreated, chronic urticaria has a severe impact on quality of life and impairs productivity by up to 30%.
• The socio-economic impact of urticaria is great, since it is a disease which primarily occurs in people of working age.
• Moderate to severe urticaria requires specialist treatment. In many health care systems worldwide, access to specialty care is insufficient.
Allergy to Drugs and Biological Agents

- Adverse drug reactions (ADR) may affect up to 1/10 of the world’s population and affect up to 20% of all hospitalized patients.
- More than 10% of all ADR are drug hypersensitivity reactions (DHR).
- Both under-diagnosis and over-diagnosis are common.
- The most common DHR involve antibiotics such as penicillins and cephalosporins, sulfonamides, aspirin and other non-steroidal anti-inflammatory drugs.
- The clinical spectrum of DHR involves various organs, timing and severity.
- DHR can be severe, even life threatening, and are associated with significant mortality rates. Drugs may be responsible for up to 20% of fatalities due to anaphylaxis.
- DHR have a significant socio-economic impact on both direct costs (management of reactions and hospitalizations) and indirect costs (missed work/school days; alternative drugs).
- Diagnostic procedures for DHR should also attempt to identify the underlying mechanisms causing the DHR.
- Diagnosis is critical for DHR management and prevention. Selection of an alternative drug and desensitization is necessary in some cases.

Insect Allergy

- Hymenoptera venom allergy (HVA) is a common global medical problem and refers to subjects who have a sting-induced large local (LL) or systemic allergic reaction. A LL reaction is defined as a reaction larger than 10 cm in diameter which lasts over 24 hours in which the signs and symptoms are confined to tissues contiguous with the sting site. Systemic reactions cause generalized signs and symptoms and include a spectrum of manifestations, ranging from mild to life-threatening. Mild systemic reactions may be limited only to the skin and consist of flushing, urticaria, and angioedema. More severe systemic reactions can involve bronchospasm, laryngeal oedema, and hypotension. HVA can cause fatal anaphylaxis.
- The morbidity rate is underestimated; fatal reactions may not be appropriately recorded, accounting for this underestimation.
- The incidence of positive specific IgE antibodies to venom is high in the general population, but only a fraction of such individuals develop a systemic reaction.
- In up to 50% of individuals who experience a fatal reaction there is no documented history of a previous systemic reaction.
- HVA impairs long-term quality-of-life (QOL) and is the cause of substantial socio-economic problems.
- A subject’s QOL is negatively affected when appropriate diagnosis and education are not achieved and when venom immunotherapy (VIT) (a series of injections of the venom to which the subject is allergic and which essentially cures their disease) is not utilized.
- HVA can be effectively treated with VIT and the appropriate venom therapies.
- HVA poses a problem in occupational settings, especially in bee keepers and greenhouse workers.
- HVA has important adverse consequences in terms of employment, earning capacity and leisure and sporting activities.
- HVA has a substantial adverse financial impact on healthcare costs.

Occupational Allergy

- Occupational allergic diseases represent an important public health issue due to their high prevalence and their socio-economic burden.
- Occupational asthma (OA) contributes significantly to the global burden of asthma, since the condition accounts for approximately 15% of asthma amongst adults.
- Allergic contact dermatitis (ACD) is one of the most common occupational disease.
- Occupational allergic diseases remain largely under-recognized by physicians, patients, and occupational health policy makers.
- Occupational allergic diseases can result in long-term health impairment, especially when the diagnostic and avoidance measures are delayed.
- Occupational allergic diseases lead to important adverse consequences in terms of healthcare resources, employment, earning capacity and quality of life.
- Occupational allergic diseases are associated with a substantial adverse financial impact for affected workers, insurance or compensation schemes, health services, and employers.
- Occupational allergic diseases are, by definition, preventable diseases and their burden should be minimized by appropriate preventative strategies.
Sports and Allergies

- Moderate and controlled exercise is beneficial for allergic subjects and should be part of their management.
- Vigorous exercise may trigger or exacerbate several allergy syndromes such as bronchospasm, rhinitis, urticaria-angioedema and anaphylaxis.
- Allergy diagnosis should be part of the routine medical examination in all professional and amateur athletes, in order to adopt adequate preventative and therapeutic measures for controlling the disease, while avoiding potential symptoms occurring on exercise.

2. RISK FACTORS FOR ALLERGIC DISEASE

The Potential of Genetics in Allergic Diseases

- Allergic disorders are heterogeneous and involve important gene-environmental interactions.
- Human genetics has a role to play in understanding susceptibility for disease onset, phenotypes and sub-phenotypes, severity, response to treatments and natural history.
- Although candidate gene association studies have provided some insight into the role of genes in disease susceptibility, most new information is emerging from hypothesis-free approaches such as genome-wide association studies.
- Genetic factors that influence the expression of atopy are different from those that influence disease manifestations or its severity in specific organs.
- Polymorphism of a single gene usually accounts for only a small proportion of the disease phenotype and risk scores using multiple genetic loci still poorly predict disease susceptibility.
- Epigenetic influences involving multiple mechanisms, including methylation of CpG islands in gene promoters and post-translational modification of histones, explain a proportion of the gene-environmental interactions and trans-generational effects.
- The genetic epidemiological observations for specific candidate genes in atopy and allergic disease require careful replication, enhanced by international collaboration and the availability of large, well-characterized case-control populations for genotyping. The only way to achieve this is to promote greater cooperation among researchers and create multidisciplinary teams including researchers from academia, industry and clinical practice.

Allergens as Risk Factors for Allergic Diseases

- Sensitization (IgE antibodies) to foreign proteins in the environment is present in up to 40% of the population.
- Such sensitization is strongly associated with exposure for proteins derived from pollens, moulds, dust mites and cockroaches.
- For asthma, rhinitis and atopic eczema there is a strong and consistent association between disease and sensitization.
- The association between sensitization to grass pollens and symptoms of hay fever occurring during the grass pollen season provides strong evidence for a causal role of grass pollen in the disease.

Environmental Risk Factors: Indoor and Outdoor Pollution

- Epidemiological studies show that indoor and outdoor pollution affect respiratory health, including an increased prevalence of asthma and allergic diseases.
- Outdoor pollution is associated with substantial mortality; ambient particulate matter and ozone pollution accounted for about 3.4 million of deaths worldwide in 2010.
- Conservative estimates show that exposure to indoor air pollution may be responsible for almost two million deaths per annum in developing countries.
- Global warming will increase the effects of outdoor air pollution on health.
- Exposure to outdoor/indoor pollutants is associated with new onset of asthma, asthma exacerbations, rhinitis, rhinocconjunctivitis, acute respiratory infections, increase of anti-asthmatic drug use, and hospital admissions for respiratory symptoms.
- The International Agency for Research on Cancer has classified the indoor combustion of coal emissions as Group 1, a known carcinogen to humans.
- Abatement of the main risk factors for respiratory diseases and, in particular, environmental tobacco smoke, indoor biomass fuels and outdoor air pollution, will achieve huge health benefits.
Socio-economic Factors and Environmental Justice

- The global prevalence, morbidity, mortality and economic burden of asthma have increased over the last 40 years.
- However, the growth and burden of the disease is not uniform. Disparities in asthma morbidity and mortality, with an inverse relationship to social and economic status, are increasingly documented around the world.
- Asthma and other atopic disorders may be more concentrated among those of lower socio-economic status because they also bear a disproportionate burden of exposure to suboptimal, unhealthy environmental conditions (e.g. physical, social, and psychological conditions).
- Future research needs to pay increased attention to the social, political, and economic forces that result in marginalization of certain populations in disadvantaged areas of the world which may increase exposure to known environmental risk factors contributing to the rising asthma burden.

Climate Change, Migration and Allergy

- The earth’s temperature is increasing as illustrated by rising sea levels, glaciers melting, warming of the oceans and diminished snow cover in the northern hemisphere.
- Climate change coupled with air pollutant exposures may have potentially serious adverse consequences especially for human health in urban and polluted regions.
- High summer temperatures have an impact on rates of acute exacerbation and hospital admission for elderly patients with breathing problems and may cause unexpected death.
- Pollen allergy is frequently used to study the interrelationship between air pollution and respiratory allergy. Climatic factors (temperature, wind speed, humidity, thunderstorms, etc.) can affect both biological and chemical components of this interaction.
- Changes in the weather such as thunderstorms during pollen seasons may induce hydration of pollen grains and their fragmentation which generates atmospheric biological aerosols carrying allergens. As a consequence asthma outbreaks can be observed in pollinosis patients.
- Migration from one country to another involves exposure to a new set of pollutants and allergens as well as changes in housing conditions, diet and accessibility to medical services which may affect migrants’ health.
- Atopy and asthma are more prevalent in developed and industrialized countries compared with undeveloped and less affluent countries.
- Migration studies provide information on the role of environmental factors on the development of atopy and asthma.
- Physicians should be aware that environmental and climate changes may enhance the development of allergic diseases and asthma.
- Physicians should be aware that migrants, especially from developing to more developed countries, are at increased risk to acquire allergic diseases and asthma and that the effect is age and time-dependent. Early age and longer time increase the likelihood of developing atopy and asthma.

3. EVIDENCE BASED APPROACHES TO DIAGNOSIS AND MANAGEMENT

Diagnosis and Identification of Causative Allergens

- Confirmation of allergy and identification of causative allergens are crucial to correctly manage allergic diseases.
- Precise diagnosis allows the implementation of therapies oriented to the etiologic factors of allergic diseases, such as environmental measures and immunotherapy.
- Diagnosis begins with a detailed medical history and physical examination.
- The identification of a temporal association between symptoms and allergen exposure constitutes the basis for further testing.
- Clinical suspicion is confirmed by means of investigation of IgE antibodies in vivo (skin tests) or in vitro.
- Skin tests should include relevant allergens and the use of standardized allergen extracts.
- In vitro testing is especially useful when skin test results do not correlate with the history or cannot be performed.
- In vitro tests can be applied to “probability of disease” prediction in food allergy.
- There is a need for increased accessibility to allergy diagnosis and therapies and improved diagnostic methodologies that can substitute in vivo provocation tests for drug and food allergy.
- The use of unproven tests increases the unnecessary costs of allergy diagnosis.
Pharmacotherapy of Allergic Diseases

- Subjects from all countries, ethnic and socio-economic groups and ages suffer from allergies.
- Asthma and allergic rhinitis are common health problems that cause major illnesses and disability worldwide.
- The strategy to treat allergic diseases is based on: (i) patient education; (ii) environmental control and allergen avoidance; (iii) pharmacotherapy; and (iv) immunotherapy.
- Pharmacotherapy is the mainstay of treatment for allergic diseases because it not only controls symptoms, but also improves the quality of life.
- Primary care physicians play an important role in the first-line management of allergies. They have to make the initial clinical diagnosis, begin treatment and monitor the patient.
- Allergy specialists are trained to make a specific diagnosis and treat patients with allergies, particularly those with moderate/severe disease.
- The chronic nature of allergies makes it essential to propose and explain long-term management strategies to patients, healthcare policy makers and government authorities.
- In recent decades, a substantial improvement has been made in the efficacy and safety of allergy pharmacotherapy.
- Disease management using evidence-based practice guidelines has been shown to yield better patient outcomes.

Allergen Specific Immunotherapy

- Allergen specific immunotherapy (AIT) is recognized as an effective treatment for respiratory allergy and Hymenoptera venom allergy.
- Subcutaneous Immunotherapy (SCIT) still represents the standard modality of treatment, but sublingual Immunotherapy (SLIT), is now accepted as a valid alternative to injections.
- SLIT is considered safer than SCIT, and its use is particularly advantageous in children.
- AIT, in properly selected patients, significantly reduces allergic symptoms and medication usage.
- At variance with pharmacotherapy, AIT induces profound and persisting changes in the immune response to allergens. This results in a long-lasting clinical effect after discontinuation and in a disease-course modifying effect (prevention of the onset of asthma and of new sensitizations).
- The mechanisms of action of specific immunotherapy are multiple and complex, and result in a modification of the immunological responses to allergens, with subsequent reduction of the allergic inflammatory reaction.
- The mechanisms of action of SCIT and SLIT are similar.
- SCIT and SLIT can maintain their beneficial effects for years after discontinuation.
- AIT indications, contraindications, limits and practical aspects are well defined in numerous guidelines.
- New forms of immunotherapy, allergen products and new indications (e.g. food allergy or atopic eczema) are currently under investigation.

Biological Agents

- Recent developments in the field of allergy and immunology have led to a variety of novel therapeutic approaches; some agents are already implemented in clinical practice, and even more agents are at the stage of clinical trials.
- New therapeutic approaches include toll-like receptor agonists, cytokine blockers, specific cytokine receptor antagonists and transcription factor modulators targeting syk kinase, peroxisome proliferator-activated receptor gamma, and nuclear factor kappa B.
- The anti-IgE mAb omalizumab has a well-documented effectiveness in patients with allergic asthma, but the criteria for selecting the patients who will benefit from it are less established.

Allergy Education for Patients and Families

- The provision of appropriate training and education for patients and families is fundamental to the management of allergic disease.
- The evidence base for the efficacy of education and training is relatively weak but it is effective in asthma and, to a lesser extent, eczema and anaphylaxis.
- Different age and ethnicity populations require different educational approaches.
- Modern information technology is valuable, especially to educate younger subjects.
- Education and training programs should contain a written self-management action plan.
Allergen Avoidance

- Effective allergen avoidance leads to an improvement of symptoms in allergic patients.
- Several studies of comprehensive environmental interventions in asthmatic children reported benefits.
- For adult asthma there is little evidence to support the use of simple, single interventions (e.g. only covering bedding) to control dust mite allergen levels.
- Similarly, in mite allergic patients with rhinitis, single mite avoidance measures are not beneficial.
- The following should be used to guide a pragmatic approach to allergen avoidance:
  - Use a comprehensive environmental intervention to achieve the greatest possible reduction in allergen exposure.
  - Tailor the intervention to the patient’s allergen sensitization and exposure status.
  - If unable to assess the level of allergen exposure, use the level of allergen-specific IgE antibodies or the size of skin test wheal as an indicator.
  - Start the intervention as early in the natural history of the disease as possible.
  - Primary prevention strategies aimed at eliminating or reducing exposure to potentially sensitizing agents should be developed and evaluated.

4. PREVENTION OF ALLERGIC DISEASES

- The rise in prevalence of allergic diseases has continued in the industrialized world for more than 50 years.
- Sensitization rates to one or more common allergens among school children are currently approaching 40%-50%.
- Strategies used to tackle these problems are thus far ineffective.
- Primary prevention is difficult because the reasons for increased sensitization rates are unknown. Also, the mechanisms involved in the progression of sensitization in increasing numbers of individuals resulting in allergic diseases are incompletely understood. Asthma and allergies may have their origin early in life, even in-utero.
- Reliable early markers of IgE-mediated diseases are unavailable.
- Novel research indicates that tolerance is the key to prevention. More research about the mechanisms involved in the development of tolerance should be encouraged. Inadequate or lack of tolerance in allergic individuals appears to link with immune regulatory network deficiencies.
- National asthma and allergy plans (e.g. The Finnish Asthma Programme 1994-2004) have concluded that the burden of these community health problems can be reduced. The change for the better is achieved as governments, communities, physicians and other health care professionals, and patient organizations commit to an educational plan to implement best practices for prevention and treatment of allergic diseases.

5. HEALTH ECONOMICS, MEDICAL EDUCATION AND COST-EFFECTIVE HEALTH CARE IN ALLERGY

Health Care Delivery and Health Economics in Allergy

- Asthma and allergic diseases are significant causes of morbidity on a global scale.
- Asthma disproportionately affects minorities and people from lower socio-economic groups.
- The total global cost of care for people with asthma and allergic disorders is disproportionately high despite the relatively low cost per person, mainly due to the high prevalence of these disorders.
- Optimal management is clearly outlined in evidence based national and international guidelines but such advice is patchily implemented.
- Shared decision making between Health professional and patient improves outcomes and doctors need to recognize the importance of support as the patient self manages their own condition.
Medical Education in Allergy
The intended outcomes for clinician and healthcare professionals training in allergy are to:

• Produce graduates equipped to further their careers in healthcare and in particular to enhance the number of individuals trained in the mechanisms and management of allergic diseases.
• Develop an understanding of the processes involved in improving the management of patients with allergic disease.
• Develop new areas of teaching in response to the advance of scholarship and the needs of vocational training.
• Provide a training in research skills.
• Develop skills and understanding of the more complex components of allergic disease encountered in specific areas of practice.

The Cost-Effectiveness of Consulting an Allergist
• Allergic diseases are chronic conditions with systemic involvement that can affect multiple organs and systems throughout the lifespan of atopic (allergic) subjects.
• In assessing the economic burden of allergic diseases, the costs of several organ-specific diseases need to be aggregated, including the nose (allergic rhinitis), sinuses (rhinosinusitis); lungs (asthma); skin (atopic eczema); and others.
• Cost-effective analyses (CEA) assess the comparative effects of one health care intervention over another, under the premise that there is a need to maximize the effectiveness relative to its cost.
• A cost-effective intervention could, if incorrectly used, generate unnecessary costs, provide no benefit and even cause harm.
• The allergist is an expert in tailoring therapy to the individual patient and adjusting treatment dosages in more severe or complex cases. The main defining characteristics of allergists are their appreciation of the importance of external triggers in causing diverse diseases; their expertise in both the diagnosis and treatments of multiple system disorders, including the use of allergen avoidance and the selection of appropriate drug and/or immunological therapies; and their knowledge of allergen specific immunotherapy practices.
• Misinterpretation of the results of diagnostic tests by non-specialists can lead to over-diagnosis and inappropriate management which can be harmful for the patient. It may lead to over-prescription of therapy and costly and unnecessary allergen avoidance measures, including exclusion diets that can lead to nutritional deficiency and secondary morbidity. Conversely, the under-appreciation of the severity of asthma can lead to life-endangering under-treatment or the lack of potentially life-altering immunotherapy.
• The cost-effectiveness of allergist consultation will be demonstrated by improved patient outcomes and experiences together with a reduction in unnecessary expenditure by payer, society or patient/family.
Declaration of the World Allergy Organization

DECLARATION

In its role as an umbrella organization of national and regional allergy, asthma and clinical immunology societies worldwide, the World Allergy Organization invited all 84 of its member societies to contribute to the White Book by participating in an online survey on the current status and needs of the specialty in their respective country or region. The responses from the Member Societies along with the scientific reviews which are included in the White Book form the basis of the World Allergy Organization Declaration.

I. Epidemiological Studies Of Allergic Diseases

Identified Need:
In several parts of the world, there is a paucity of published epidemiological information about the overall prevalence of allergic diseases and, in particular, about specific diseases. For example, there is little or no information about severe asthma; anaphylaxis; food allergy; insect allergy; drug allergy; and complex cases of multi-organ allergic disease. Data concerning some of these disorders are available in a few countries, but only for certain age groups.

Recommendation:
Every country should undertake epidemiological studies to establish the true burden of allergic diseases; asthma; and primary and secondary immunodeficiency diseases. This is the first essential step in ensuring the provision of adequate physician and healthcare professional services to meet both current and future needs.

II. Allergens And Environmental Pollutants

Identified Need:
Evidence-based information about the major indoor and outdoor allergens and pollutants responsible for causing or exacerbating allergic diseases and asthma is either lacking or, when available, is not always universally accessible.

Recommendation:
Local indoor and outdoor allergens and pollutants which cause and exacerbate allergic diseases should be identified and, where possible, mapped and quantified. Appropriate environmental and occupational preventative measures should be implemented where none exist or as necessary. Strategies proven to be effective in disease prevention should also be implemented.

III. Availability Of Allergy, Asthma And Clinical Immunology Services (Allergists) And Appropriate Medications

Identified Need:
There is an increasing need for more allergy specialists and for the existence of local and regional allergy diagnostic and treatment centers in order to facilitate timely referrals for patients with complex allergic diseases. Accessibility to affordable and cost-effective therapy and to novel therapies is needed. For example, adrenaline auto-injectors for patients at risk of anaphylaxis; new and more effective medications to treat severe asthma; and access to allergen immunotherapy are lacking in some parts of the world.

Recommendation:
Public health officials should provide for adequate allergy/clinical immunology services, including access to specialists and diagnostic and treatment centers. Allergists should be able to prescribe the most cost-effective medication to manage a patient’s disease. Examples include adrenaline auto-injectors to treat anaphylaxis; anti-IgE for severe asthma; a variety of very effective medications to treat chronic urticaria and angioedema, hereditary angioedema, rhinitis, conjunctivitis and asthma.
Allergen-specific immunotherapy is effective in preventing the onset of asthma and is the only available treatment to prevent anaphylaxis and death from bee, wasp, yellow jacket, hornet and ant induced anaphylaxis. Consultations with allergists, timely diagnosis and treatment are necessary to improve long-term patient outcomes and quality of life and to reduce the unnecessary direct and indirect costs to the patient, payer and society.

IV. Undergraduate And Postgraduate Education For Primary Care Physicians And Pediatricians

Identified Need:
There is a need for undergraduate and postgraduate training in allergy, asthma and clinical immunology for general practitioners and pediatricians such that primary care physicians and pediatricians may appropriately assist patients with allergic diseases.

Recommendation:
Allergic diseases are a major cause of morbidity and mortality. Suitable undergraduate and postgraduate training for medical students, physicians, pediatricians and other healthcare professionals will prepare them to recognize allergy as the underlying cause of many common diseases. It will also enable them to manage mild, uncomplicated allergic disorders by targeting the underlying inflammatory mechanisms associated with these diseases. They will learn when and how to refer the more complicated cases for a specialist consultation. Such education at the general practice level is of paramount importance since the vast majority of patients with allergic diseases are cared for by primary care physicians and pediatricians. These clinicians will also be required to co-manage such patients with an allergy specialist and should be aware of the role of the allergist/clinical immunologist in investigating, managing and caring for patients with complex allergic problems.

V. Recognition Of The Specialty And Training Programs

Identified Need:
Globally, medical education providers need to recognize allergy / clinical immunology as a specialty or sub-specialty, resulting in adequate training programs for optimal patient care.

Recommendation:
Expertise in allergy and clinical immunology should be an integral part of the care provided by all specialty clinics. Where allergy/clinical immunology training is not presently available or recognized as a specialty, training and national accreditation programs should be instituted to enable selected physicians to receive formal training and the qualifications required to become certified allergists/clinical immunologists. Such programs will also enable general practitioners, including pediatricians, to enhance their capacity to provide for the routine care for patients with allergic diseases.

VI. Public Awareness Of Allergy, Asthma And Clinical Immunology

Identified Need:
In most populations around the world, there is a lack of adequate education about, and awareness of, the morbidity and mortality associated with allergic diseases; the often chronic nature of these diseases; the importance of consulting a physician trained in allergy, asthma and clinical immunology; and the medications and treatments available to appropriately treat and prevent these diseases.

Recommendation:
Public health authorities should target allergic diseases as a major cause of morbidity and potential mortality. They should collaborate with national allergy, asthma and clinical immunology societies and patient support groups to publicize the necessity for general awareness and appropriate care for these diseases.
Conclusion

The World Allergy Organization (WAO) is an international umbrella organization whose members consist of 92 regional and national allergology and clinical immunology societies from around the world. These regional and national societies are an excellent resource for knowledge and expertise. It is strongly recommended that public health and government officials, medical school leaders and patient groups collaborate with these societies to promote excellence in care for patients with allergic diseases.

As members of the World Allergy Organization, the regional and national allergy, asthma and clinical immunology societies contribute to the work of the WAO Councils and are available to assist with enquiries about how best to implement these recommendations. Information is available on the WAO website www.worldallergy.org and enquiries may be directed to info@worldallergy.org.
Check out the updated White Book on Allergy!