

Abstract, Executive summary, Extracts

EUROPEAN
ALLERGY
WHITE
PAPER

ALLERGIC DISEASES
AS A PUBLIC HEALTH PROBLEM
IN EUROPE



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THE INVASION OF EUROPE HAS STARTED

They are in the air we breathe, the food we eat, the water we drink and the beds we sleep in: microorganisms and organic molecules. Acting by various mechanisms, foreign substances of various origins can invade the body and cause a hypersensitive reaction of the immune system, called allergy.

While allergy does not enjoy the morbid fascination of AIDS, cancer or cardiovascular diseases as a major killer, it is certainly one of the most pervasive disorders globally. Allergic conditions now pose a major health problem. They respect no national frontiers and are spreading inexorably through the European population.

In an appropriate initial response to this Pan-European invasion, the UCB Institute of Allergy has enlisted the help of leading allergologists across the length and breadth of Europe and compiled a meta-analysis of the problem in the European perspective. This border-crossing European Allergy White Paper paints a disturbing picture of the gathering pace of the allergenic invasion. The following synopsis sketches the main points, but in essence it should be seen merely as a paintbrush moving over the canvas of a medical problem of truly global proportions.

Keywords

Epidemiology - Rhinitis - Asthma -
Atopic Dermatitis - Food Allergy -
Children at Risk - Diagnosis - Treatment -
Prevention - Socio-economic Costs and Implications -
Organization of Health Care - The Way Forward

EXECUTIVE SUMMARY

Allergic diseases most commonly occur as rhinitis, asthma, atopic dermatitis and other skin complaints, but also as life-threatening anaphylactic shock. In developed countries they are among the commonest chronic disorders, affecting up to 15-30% of the population. The disparity of the organization and resources for the delivery of health care to allergics in EU countries has tremendous social and cost implications. The paper documents the scope of allergic diseases in Europe. It describes current approaches to allergy diagnosis, treatment and prevention and outlines methodologies for a unified approach to successful health care delivery

Numerous studies show a dramatic increase in atopic syndrome diseases in recent decades, while epidemiological surveys demonstrate that the rapid increase in allergic diseases is a real phenomenon. Various factors and complex environmental interactions are involved, including the quality of housing, different feeding habits and our changed industrial and chemical environment. Epidemiological research focused on the possible causes of these changes is crucial for a rational and economic approach to preventive or curative interventions.

During the past two decades our understanding of allergic diseases has improved considerably, but concurrent rapid changes in the environment and people's lifestyle have generated hitherto unknown allergies which may assume wide proportions.

While allergies such as hay fever were once looked upon as minor nuisance disorders, this banal outlook is changing. Firstly, diseases affecting every third member of a community cannot be disregarded. Secondly they severely impair the quality of life over a prolonged period, causing lost productivity and workdays. In many countries they have a major negative impact on the burden of socio-economic costs. Addressing these problems has become imperative for public health authorities.

Lastly, while disease prevention rather than just therapy is clearly a major goal, achieving it is rendered difficult by the complexity of the factors involved. Nevertheless, current research offers a realistic hope, but greater awareness is needed across the European medical spectrum to develop coherent public health approaches to the problem of allergies.

ALLERGOLOGY IN PRACTICE

This paper is therefore concerned principally with the allergic diseases provoked by exogenous non-infectious agents which are inhaled, ingested or injected, or which come into contact with mucosal surfaces. Allergies which are discussed include summer hay fever, perennial rhinitis, allergy to stinging insects, allergy to drugs, allergy-related skin disorders, food allergy and intolerance, anaphylaxis, and evaluating the role of allergy in non-specific/polysymptomatic illness.

Allergy plays a major role in many asthmatics for part of the time, but in some cases of urticaria (hives) it probably plays only a minor role. Rhinitis can have both allergic and non-allergic causes. Seasonal allergic rhinitis (summer hay fever) is entirely due to allergy. The allergens in chronic allergic rhinitis are usually house-dust mites and animal dander, but numerous cases of chronic

rhinitis have no underlying allergic cause. In many patients with food-related symptoms, some have true food allergic disease but in others there is no evidence that it is associated with a change in the immune system; 'food intolerance' may therefore be a more appropriate term.

The importance of allergy can also change over time: in atopic eczema, for example, allergic factors appear to be more apparent in children than in adults. A major role of the allergologist, therefore, is to evaluate the respective role of hypersensitivity versus non-specific mechanisms in the origin of the symptoms, since this markedly affects therapy and prognosis. However, this presupposes diagnostic skills and approaches which are not yet generally in place or uniformly practised in the European Union.

Allergic rhinitis

There is increasing evidence that the frequency of allergic diseases has increased world-wide over the past few decades. Allergic rhinitis is a classic example. Non-infectious rhinitis may be either chronic or recurrent and occur either seasonally or perennially; but despite it being one of the most common allergic disorders, there are still unanswered questions as regards its epidemiology.

When a causative agent can be identified, rhinitis is labelled 'allergic'. Such seasonal rhinitis is generally caused by an allergic reaction to inhaled grass pollen (hence the name 'hay fever') and is easily identified as allergic. However, owing to the relatively small percentage of patients seeking professional advice for rhinitis, population studies show that its prevalence is nearly twice as high as in studies conducted in general practice.

The frequency of hay fever has increased considerably since the beginning of the 20th century where it was of the order of 1%; overall prevalence in the general population now approximates 15-20%. In young children the prevalence is relatively low but rises rapidly, peaking in late adolescence/early adulthood and then declining steadily with advancing age. There are local or regional differences in the prevalence of hay fever as well as in the possible causal allergens.

Recently, urban air pollution, especially due to noxious emissions from motor vehicles, has been increasingly incriminated as one of the potential causative agents. This theory, however, is disputed by many observers. Other factors postulated as causal in the increasing prevalence of hay fever include ethnic sensitivity, social class, family size, and maternal smoking.

Although allergic rhinitis remains an *undiagnosed* and *undertreated* disease, it should not be discarded as a minor nuisance. Recent studies clearly show that allergic rhinitis of the perennial type usually due to indoor aller-

gens leads to as much if not more impairment of the patient's quality of life (and by extension that of his partner and environment) than mild or moderate asthma. Some studies even suggest that allergic rhinitis is often a gateway to asthma.

Allergic asthma

The diagnostic problems associated with asthma are perhaps best illustrated by the fact that the World Health Organization, the American College of Chest Physicians/American Thoracic Society and the National Asthma Education Programme Expert Panel Report all give a different definition of the disease concept.

Apart from a high prevalence of transient infection-induced bronchial obstruction during the first years of life, two-thirds of children become asymptomatic before school age, but there is subsequently a tendency towards increasing prevalence with growth into adulthood. In general, the male-female prevalence ratio is 2:1 in early childhood, gradually equalizing with advancing age.

Recent studies show that the prevalence of asthma has increased, with most authors indicating an approximately twofold increase in the 1980s. Nevertheless, despite this increase, mortality in Europe has remained low compared with other parts of the world. Interestingly, and disturbingly when viewed in the longer term, especially where children are concerned, *unidentified factors related to our modern 'western lifestyle' appear to be the strongest determinant in the development of asthma.*

Several studies show a higher prevalence of asthma in both children and adults in urban areas, which may be due to the above-mentioned western lifestyle and outdoor air pollution. In contrast to allergic rhinitis, and this is a stark reflection on life in our civilized society, asthma is generally more severe among the socially disadvantaged than in the higher socio-economic groups.

Atopic dermatitis

Atopic dermatitis is a coat of many colours, and differential diagnosis is sometimes difficult to make. As a result, there is considerable disparity in prevalence data in the professional literature. Nevertheless, diagnostic criteria have been proposed and they have gained wide international acceptance. The epidemiology of atopic dermatitis was recently summarized in major reviews which reached, *inter alia*, the conclusion that the cumulative incidence of atopic dermatitis before age seven has increased dramatically during recent decades and that 10 to 20% of children with this disease develop asthma.

A major review encompassing 25,000 children in five European countries shows that atopic dermatitis is now a major public health problem in Europe. In some places prevalence rates are as high as 24%. The risk of developing respiratory symptoms in later years is around 40 to 60%. And there is irrefutable evidence that atopic dermatitis will specifically be a major health problem for children born after 1980.

Allergic contact dermatitis

Knowledge of the prevalence and incidence of contact dermatitis is fragmentary. Routinely registered data are not informative because this disease is seldom a cause of hospitalization and patient populations from dermatology clinics represent but a small proportion of the true incidence. However, from major population studies conducted in the US and in EU countries, the prevalence of allergic contact dermatitis in the general population is estimated at 1%.

Food allergy

Increasing public awareness of the relationship between diet and health has led to the assumption that many foods cause allergy. In fact, a recent epidemiological study in the UK indicates that over 20% of the popula-

tion share this belief. Examination of such patients shows, however, that the true incidence of food allergy is certainly lower, about 2-3% of the population.

One of the major obstacles to diagnosing food allergy is the lack of reliable *in vitro* diagnostic tests and the fact that provocation tests are often based on subjective parameters. However, this problem may soon be solved, thanks to recent advances in the development of new scientifically sound diagnostic procedures.

A clear distinction must be made between food allergies arising in early infancy and in adulthood. While it may be postulated that infantile food allergy is the gateway to allergy at a later stage in life, nevertheless there are relatively few studies on the prevalence of food allergies in adults. Indeed, at present there is but little reliably documented data indicating whether the overall prevalence of food allergy has changed in recent decades.

Prevalence and change are very dependent upon public awareness as well as changes in eating habits. The increasing availability of potent allergenic foods, such as exotic fruits, has brought an inwards migration of food allergies to Europe, whereas the familiar cow's milk allergy seems to be decreasing from its peak at the beginning of the 20th century, possibly in conjunction with the renewed popularity of breast-feeding and the use of cow's milk hydrolysates.

Foods implicated in hypersensitivity therefore vary according to patient age, geographical region and eating habits. However, studies have yielded evidence that 15 to 30% of allergic infants remain allergic to milk and/or egg for longer periods, while allergy to peanut and fish appears to persist for several years in the majority of cases. Food allergies in adults may appear at any age, sometimes in association with a bowel disease.

Drug allergy

The best sources of epidemiological data are surveys within the framework of drug monitoring programmes, because unfortunately (and surprisingly) *there are almost no systematic studies describing incidence and prevalence of allergic and pseudo-allergic reactions to drugs* in a general population. The major forms of allergic and pseudo-allergic reactions have, however, been identified; but one of the major problems with drug allergies is that their frequency will be regionally affected by doctors' prescription modes, which are quite variable, and also by the rapid changes resulting from the momentum of scientific research in the international pharmaceutical industry. Forty percent of all life-threatening anaphylactic reactions are due to drugs.

Major allergens

Different climates and indoor and outdoor environments strongly influence the geographical distribution of major allergens. Some allergens have particularly potent sensitizing effects and may lead to monosensitization, although multiple sensitivities are more usual in atopic patients. The presence of major inhalant allergens in the outdoor environment of most European countries is reported by aeroallergen survey stations and compiled by the European Aeroallergen Network. Outdoor allergens such as pollen and spores are the causative factors in a high percentage of hay fever and asthma cases. The major indoor allergens are house-dust mites and animal dander.

Biological markers

Skin-prick testing, the most frequently used biological marker for the presence of IgE-mediated hypersensitivity and the atopic syndrome, is not a very reliable technique and may give very different results in the hands of different investigators. Furthermore, a sizeable proportion of the population may yield positive skin tests even in the absence of allergic symptoms and disease.

Determination of total and allergen-specific IgE is since 30 years an important objective element of allergy diagnosis. Epidemiological studies based on IgE determination confirm the high incidence of atopic sensitization in Europe at about 30% as well as its recent increase.

A number of cellular studies on random cord blood leukocytes have shown that some state of hypersensitivity is already present at birth in selected newborns. However, while such methodologies are still too cumbersome or costly for large epidemiological studies, the development of cytoflowmetric techniques for the detection of allergen-induced cellular activity may be considered in the future.

Genetic aspects

The most impressive evidence for a genetic effect in the development of atopy is derived from twin studies which indicate that as much as 50% of the variation in IgE levels is attributable to genetic factors.

It is encouraging to note that *the development of molecular genetics should eventually enable us to recognize the basis of family patterns* of symptoms and other biological markers. So far, genetic studies have mainly been conducted on selected patient populations and atopic families and have been based on apparent phenotypes, i.e. an identifiable or observable structural or functional characteristic of an organism. The next step will be to assess the prevalence of molecularly defined genetic markers and their impact on disease. This may lead to new and interesting prospects for diagnosis and therapy.

Outdoor pollution

The occurrence of an asthma 'epidemic' in modern industrialized societies world-wide is well documented, albeit controversial, but the causes of the twofold increase in the past 20 years have not yet been identified. Evidence of an association between air pollution and

health outcomes in the general population can be found in the rates of epidemic mortality in patients already affected by asthma or chronic bronchitis. (Cf. the mortality rates in the 1950s and early 1960s during the notorious London smog era). However, as already intimated, there are different schools of thought about the part played by air pollution in the development of allergy.

The reunification of Germany offered a unique opportunity to study the impact of environmental factors on the development of allergic diseases. Surprisingly, prevalence of asthma and hay fever was significantly higher in West Germany than in East Germany. Two different types of air pollution were then postulated as being causal factors: industrial pollution in Eastern Europe leading to bronchitis and automotive pollution in the West leading to allergy. There may be, however, as discussed below, other factors involved to explain the differences.

Studies have yielded evidence that air pollutants and volatile organic materials are major causes of exacerbation of asthma, and therefore responsible for increased medical costs through disability, as well as impaired lung function and reduced quality of life.

Indoor pollution

Some of the major allergens are encountered indoors. In warm and humid climates and houses, in particular, house-dust mites are the most common allergen and have been incriminated as a major contributing factor to the increased prevalence. Other sources of indoor allergen exposure, such as pet animals, are coming under increased scrutiny. Maternal smoking is another factor which may act as an auxiliary factor for sensitization.

Smoking affects the airways and there is increasing evidence that passive smoking may cause a health-threatening form of pollution, especially in terms of allergic sensitization and IgE formation. Children living with parents who smoke have a higher frequency of allergy to

indoor allergens than children growing up in smoke-free homes.

Lifestyle, habit and preventive measures

Changes in lifestyle and habit may also be causal factors in the recent increase of atopic diseases. Abolition of early Bacillus Calmette-Guérin vaccination (BCG) in Western European countries, for example, appears to have coincided with the increase in IgE-mediated diseases.

The present international consensus suggests that other risk factors may be strongly linked to the modern western lifestyle, possibly including such factors as a gradual decrease in the ability of our immune system to repulse invading microorganisms and increasing contact with chemicals and industrially processed foods. Most evidence favours the hypothesis of adverse effects due to an increasingly hygienic and artificial antigen-producing environment. However, preventive measures against major indoor allergens should reduce morbidity significantly.

Future epidemiology

In some regions, about half of all children and young people are now affected with allergy - *and we do not know the potential size of the susceptible population.*

Early recognition of trends to determine the negative or positive environmental impact remains a primary concern, requiring epidemiological studies and repeated monitoring of incidence and prevalence both at regional and national level, and ideally on a Pan-European scale.

DIAGNOSIS AND TREATMENT

Allergy is one of the most common chronic diseases in Europe - *and the prevalence is increasing*. GPs should therefore be able to recognize and correctly manage any urgent allergic distress. National and international bodies have recently developed consensus guidelines for the management of allergies. The major aspects of these guidelines relevant to optimal practice, and their impact on socio-economic aspects of allergic diseases, are summarized below.

Diagnosis

While clinical diagnosis is usually a simple matter, some patients require more sophisticated investigation. Critical evaluation of the patient's clinical history is needed in order to avoid a misleading interpretation of laboratory tests.

Most European allergologists and physicians initially use skin-prick tests to identify the allergens suspected on the basis of the clinical history. However, presumably due to the lack of standardization of allergenic extracts, there are still differences among allergologists as regards the performance of skin tests and interpretation of the results. Moreover, in several countries GPs are allowed to perform skin tests and treat allergic patients without specialist advice, leading to the risk of incorrect performance and interpretation of skin tests as well as inappropriate, expensive and sometimes even harmful treatment.

Measures need to be taken by European and national health care authorities to restrict the practice of skin tests to physicians who have been formally trained in their use and interpretation.

Allergy management: avoidance, treatment and immunotherapy

Allergen avoidance is obviously the first line of treatment, e.g. avoidance of pets, but patients are not always

cooperative. In food allergy, occupational asthma and drug allergy, too, avoidance is the first line of defence.

Equally important, all European physicians and allergologists should be acquainted with sound principles of avoidance exposure.

Drug treatment

Pharmaceutical R&D has produced significant new achievements in the drug treatment of asthma and allergic diseases in recent decades. Apart from H₁ receptor antagonists, the most frequently prescribed drugs in Europe are selective β₂ agonists and inhaled corticosteroids.

It should be noted, however, that where the steroids, topical antihistamines and cromoglycates are concerned, there are major differences in prescribing and frequencies among some European countries. And despite the international consensus and guidelines for the treatment of these diseases, such as bronchial asthma, there are also significant differences in patient management, due in part to non-specialist treatment. Quite apart from the need for wider distribution and application of these guidelines, treatment should be effected in close cooperation between GPs and specialists.

Immunotherapy provides some protection against the effects of natural allergenic exposure by providing regular administration of the causative allergens (desensitization). It is usually performed by injections of the relevant allergen, gradually titrated to the optimal dose. Immunotherapy is usually efficacious, but this treatment - which is used variously in EU countries - does have to be administered under the careful supervision of a trained physician and with the standby support of emergency treatment.

Quality of allergen extracts compromised?

The quality of allergen extracts (AEs) used for skin tests and *in vitro* assays is central to their reliability and is consequently of fundamental importance. It is therefore disturbing to note that *standardisation of AE quality among the EU countries is not yet a full reality*.

Over the past two decades, the development of standardization methods for AEs in Europe has been driven by

the manufacturers and not by the authorities. This evolution, engendered by a lack of national and European guidelines until quite recently, has an ongoing negative impact on cost containment and the quality of customer service. It represents another challenge to Pan-European health care: to achieve convergent implementation of EU directives for biological standardization of allergen extracts.

PREVENTION OF ATOPIC DISEASES: CHILDREN AT RISK

Atopic diseases (multifactorial disorders in which genetic components and complex environmental factors contribute to the aetiology) put about 10-20% of the population at risk. Three different levels of prevention are proposed: primary (children at risk without the disease), secondary (individuals with markers or early indicators of the disease) and tertiary prevention (patients with evidence of chronicity).

A recent study has shown a *high risk potential among newborns*. In Germany, for example, only 58% did not have an increased risk for atopy. Even more startling, if recently proposed primary prevention methods were to be accepted, *more than one-third of all newborns in Europe would be classified as potentially atopic* and candidates for preventive interventions.

Indoor allergen exposure is a risk factor for early sensitization. As infants and young children spend 90% of their

time indoors, they are commonly exposed to indoor allergens earlier than to outdoor allergens. There is especially close contact with house-dust mites and pet dander, the latter being significantly associated with asthma. Moulds may also contribute to the allergen counts in indoor air.

The detrimental effects of passive smoking have already been mentioned, but they have special relevance here because the morbidity of offspring during infancy was reduced after mothers stopped smoking during pregnancy. The paper concludes by advocating breast-feeding during the first months of life, improved ventilation in houses, avoidance of pets (also in day-care centres and schools), avoidance of smoking and passive exposure during pregnancy, and a total ban on smoking in public places.

ORGANIZATION OF HEALTH CARE FOR ALLERGY PATIENTS

Health care throughout Europe is in the process of radical change, with the European GP increasingly assuming the role of health-care gatekeeper. This has considerable implications for the diagnosis and treatment of allergic disease.

A concept like 'European Good Allergy Practice' presupposes well-founded answers to incisive questions such as 'What is the nature of the health care systems (HCS) for allergies in the various EU member states?'; 'Does the HCS specifically provide for specialized allergology measures?'; 'Is there a special set of costs for tests that can only be performed by specialists in allergic diseases?'; 'Does the HCS provide direct access to and free choice of a specialist for allergies?'; 'Who carries the burden of caring for allergies?'; 'Are specific allergological medical interventions reimbursed by the HCS?'; 'Does the HCS take into account the indirect costs of allergic diseases?'

An appropriate response to these questions, and other measures, may have a profound impact on the quality of allergy care but also on reducing the ultimate cost of allergic diseases to society as a whole. However, only fragmented information is currently available on such costs and on the cost-benefit ratio of measures affecting indirect costs of allergic diseases in Europe.

A geographic breakdown of 12 European countries highlights the disparity in approach, again emphasizing that the EU still has a long road to travel to true unification. In some countries allergology is a specialty in others merely a sub-specialty. The uncertain lines of demarcation of many clinical activities that such a dichotomy presents, and the disparity of research funding across Europe, serve to exacerbate the allergy problem rather than promote the interests of asthma and allergy sufferers.

The paper gives background details of present allergology practice in Europe and proposes workable *modus operandi* from which a more positive picture emerges than the current status, thanks to improved medical education in allergy and better adult and paediatric allergology practice - promoting in every respect better health for asthmatics and allergics.

The manifold recommendations made by the paper range from harmonized structuring of the organization and resources for the prevention and treatment of allergies, to making relevant postgraduate training programmes available across the European landscape and improving collaboration between GPs and specialists.

The authorities responsible for the governance of the EU should be aware of the complex and important problems involved in the diagnosis and treatment of allergies.

Furthermore, they should all recognize the urgent need to provide more capital to fund not only research but also a system of centralized cross-border coordination in Europe, aimed at standardization of teaching and training in allergology and clinical immunology

An increasingly important role is also played by the lay organisations of allergic patients learning to cope better with their allergies.

THE SOCIO-ECONOMIC TOLL

Health care providers and authorities in Europe are becoming increasingly aware that allergic diseases represent a major and increasing factor in public health costs. These costs are difficult to estimate due to lack of adequate data. Nevertheless, *it is estimated that the yearly direct and indirect costs of allergies in Europe amount to 29 billion ECU.*

The socio-economic cost of allergic diseases is not structured like that of the major killers. And allergic diseases are seldom fatal. Nevertheless they impair the quality of life over a prolonged period, resulting in a continuous drain on public health resources, loss of workdays and

many other cost items. The manifest distress of asthmatics probably explains why most studies and surveys on (the cost of) allergy have primarily focused on asthma.

For a proper evaluation of the effective socio-economic cost, numerous and diverse factors must be considered, including direct and indirect costs, which vary from one type of allergic disease to another. In a word, a more sophisticated approach is needed, one which also takes account of the inverse relationships between some of the cost factors.

DEVELOPING NEW STRATEGIES

For a better assessment of the cost-benefit ratio of new therapeutics or management measures, it would be useful if figures and costs related to the major allergic diseases were included in all statistics from health providers. New antiallergics should be evaluated not only in terms of their immediate beneficial effect on symptoms and comparative costs, but also with respect to their impact on the quality of life and the long-term reduction of direct and indirect costs.

Lastly, greater attention should be focused on the effect of medical management of allergies on indirect costs, especially on the cost-benefit ratio of preventive and allergen-avoidance measures, as well as on the cost of education and patient self-management programmes.

In addition to environmental measures in general, *the*

most cost-effective ways of effectively addressing the increased prevalence of allergic diseases - while at the same time limiting their cost to society - are preventive and educational support measures.

Sadly, in Europe today most allergy patients are still *improperly diagnosed and undertreated*. Allergy is a growing problem which has a major impact on occupational performance and the quality of life - both that of the patient, his family and others in his environment. Major efforts are needed to redress this situation; initially generating additional expenditure for health care systems but ultimately reducing the cost of allergenic care to society as a whole.

These efforts must be initiated without delay, to prevent this problem spiralling out of control.

The way forward

The organization of health care needs to be restructured on a national or supranational basis, to provide greater uniformity and effectiveness of health care systems and professional training in allergology. Systems of high-quality assessment must be introduced, as well as Chairs of Clinical Allergology. Other innovations regarded as imperative are interdisciplinary Centres for Allergology and scientifically based, statutory preventive measures with proven efficacy. Lastly, *validated guidelines for diagnosis and treatment are central to a revitalized Pan-European approach to allergic diseases.*

Prevention requires, *inter alia*, more precise identification of atopic individuals and risk factors in the aetiology of atopic disease. Pollen counts should be made publicly available throughout Europe, while an evaluation of measures for primary prevention is likewise considered essential. The efficacy of promising pharmacotherapeutic agents and immunotherapeutic regimes in secondary prevention should be evaluated.

Attention should also focus on new ways of building and ventilating houses, public buildings and factories, and there is a need for a precise declaration of all food contents and everyday consumables. Lastly, general health education programmes for the population, especially for pregnant women and schoolchildren, need to be introduced.

Where research is concerned, it is essential to achieve a better understanding of the development of target-organ hyperresponsiveness and tissue damage leading to long-term complaints and morbidity - with the aim of gaining a better understanding of treatment targets. *In the final analysis, it means that basic research will come under increasing pressure and it will only be possible to achieve our common goal with adequate funding.*

Diagnostic techniques will have to be improved - and the most reliable tool is a diagnostician in the true meaning

of the word. Standardization of allergic preparations should be governed by a single, internationally accepted system, while test systems should be evaluated for their diagnostic relevance. Measuring allergen exposure will become increasingly important, as too will the impact of newly identified allergens. In the investigative sphere, cells, mediators, cytokines and soluble adhesion molecules should be further studied for their value as markers for clinical and research purposes.

Therapy targets fall into four categories: down-regulation of inflammation, relief of symptoms, avoidance of exacerbation and maintenance of the quality of life. *These targets will have a considerable impact on the near-term treatment of allergy and on the associated health budgets.*

To meet all the different demands made of antiallergic and symptom-relieving compounds, innovative drugs need to be developed and extensively studied. Antagonists to mediators other than histamine are already emerging from basic research, while the new research field of cytokines and adhesion receptors offers interesting prospects. Selective markers for predictive therapy outcome are also needed; efforts are already being made to improve the efficacy of immunotherapy and such markers may give greater prominence to the role of immunotherapy in the future.

Constructive cooperation between the pharmaceutical industry and academic circles should be stimulated with a view to developing new therapeutic strategies. To end on an optimistic note, new strategies are currently in preparation which may successfully counteract IgE hyperresponsiveness at some time in the future.

The medical community, the pharmaceutical industry and the authorities responsible for the governance of the European Union - and indeed the citizens themselves - are facing a daunting yet ethically unavoidable challenge: to stem and repulse the allergenic invasion of Europe.

