

Towards prevention of allergy through an integrated multidisciplinary approach

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Abstract

Both food- and environmentally-related allergies are a continually growing health problem, particularly in the western world. The exact causes and the additional environmental and social factors that play a role in the onset of these illnesses are still poorly understood. While sufferers of allergy remain a minority in society, the reduction of their quality of life and the financial consequences for society as a whole are of major significance. Allergy is an illness that confronts the sufferer on a daily basis with his or her life style limitations. The direct and indirect annual costs to society (medical care, sick leave, loss of earnings, reduced productivity) are already running well into billions of euros. A complicating factor is that there are many kinds of allergy, with many different causes, requiring several approaches for treatment. There is no single solution. Much social and scientific research is still needed to generate additional knowledge required to determine a suitable multidisciplinary strategy for the long-term tackling of this problem. Input from a wide range of sources, including social scientists, medics, agronomists and immunologists, is essential to fully assess the situation and to assist in determining long-term policy decisions at a national level. This multidisciplinary calls for broad support from different sections of government, industry and societal bodies to achieve the desired goal of reversing the rise in the number of allergy sufferers, preferably through prevention rather than cure. In this article we present the most salient items from the presentations and discussions of a workshop on the agronomic approaches to allergy prevention, recently held in the Netherlands.

Additional keywords: hay fever, food allergy, oral allergy syndrome, coeliac disease

Introduction

During the last three decades, the prevalence of allergy has increased significantly both in number of cases and extent of individual cases. Allergy has been called ‘the

epidemic of the 20th century' (Anon., 1997). Various allergic responses can be distinguished of which asthma, rhinitis, eczema and food allergy are the most common ones. These types of allergy are so-called IgE (Immunoglobulin type E) -mediated allergies, which are different from cell-mediated allergies, prominently typified by e.g. coeliac disease, or gluten intolerance.

Currently, most attention is being paid to medical *treatment* of allergic patients. However, there is a growing awareness that *prevention* of allergy deserves much more attention. Compared with treatment, prevention during the pre-medical phase will be much more effective in reducing the costs of health care and in improving the patients' quality of life. In the light of this, several research initiatives have recently been started, financed by the Dutch Ministry of Agriculture, Nature and Food Quality, and by Wageningen University and Research Centre. Allergy prevention involves many aspects of society and therefore needs a multidisciplinary approach, with integrated and well co-ordinated activities in the fields of research, education and communication. This has only been recently recognized and is the reason behind the establishment of e.g. the Allergy Consortium Wageningen (ACW).

The ACW approach is characterized by its strong and unique focus on allergy prevention through a source-based approach, which includes the development of integrated and multidisciplinary strategies for allergy prevention and management during the pre-medical phase. The strategies chosen are directed towards the control of allergens both in food and the environment. Basic activities for strategy development are research, education, and information transfer related to primary production (plant, animal), food technology and food production chains, the living and occupational environment, as well as societal aspects (related to patients, consumers and governmental and industrial stakeholders).

To discuss experiences and opinions on allergy in an agronomic context a workshop was organized in 2003 within the framework of the research programme 'Plant Compounds and Health' financed by the Dutch Ministry of Agriculture, Nature and Food Quality (LNV-DWK 408). The workshop was attended by representatives from about 40 different organizations, including three ministries, medical and agricultural research institutes, patient and consumer organizations, pharmaceutical and food industries, and journalists. Presentations were given on immunological research, patient concerns, the viewpoint of the food industry and speciality markets, macro-economic aspects, and an overview of a recently started research programme on approaches to allergy prevention in an agronomic context. Finally, the workshop participants discussed a number of statements concerning allergy prevention from different angles of society. The results of this workshop are embodied in this article.

What is allergy?

Allergy includes all excessive reactions of the immune system to compounds that are normally tolerated by the human body. Usually, when the immune system for the first time comes into contact with compounds – especially proteins – that can elicit an immune response, such compounds prime the immune system. These compounds or

'antigens' can originate from the living environment (airborne from small arthropods such as dust mites, dandruff from pets, pollen), from plant- and animal-derived foods, or from materials coming into direct contact with the skin (e.g. latex). The human immune system will react to these antigens through the production of antibodies (immunoglobulins (Ig) of various types) that are highly antigen-specific. Frequent contact with such antigens generally results in tolerance of the immune system to the antigen, i.e., the immune system no longer considers these antigens as a threat to the body. So tolerance refers to a state of unresponsiveness in which the production of antibodies is not stimulated.

However, many individuals have a specific genetic predisposition that, in combination with certain environmental factors, results in this state of unresponsiveness failing to occur. Such people are called 'atopic' and have increased concentrations of a certain antibody (IgE) in their serum. In these cases, contact with specific antigens results in sensitization, which can lead to the production of specific antibodies against a normally harmless antigen. Their general health may quickly become affected and the person becomes 'allergic'. The word allergy means 'altered reactivity' (*allos*, different; *ergon*, work) and allergy can be considered as a false alarm of the immune system. The antigen has become an allergen and the antigens then become responsible for the occurrence of the inflammatory symptoms typical of most allergic reactions.

Allergen exposure in the nose, eyes or frontal and nasal sinuses will result in rhinitis. An example of such a reaction is hay fever but similar symptoms may also result from proteins in animal dandruff, hairs and feathers. Exposure of allergens to the skin can cause eczema (dermatitis), which is a long-lasting inflammation of the skin cells. In the case of asthma, the bronchial tubes and lungs become inflamed, which, through swelling of the mucous epithelium, results in bronchial stricture and potentially life-threatening respiratory problems. Responses of the digestive tract, resulting from contact with food allergens, can cause diarrhoea and vomiting. In some cases, like the nut allergies, this can rapidly result in anaphylaxis, an acute and potentially fatal reaction. A specific and commonly occurring case of food allergy is the 'oral allergy syndrome' (OAS). Itching and swelling of the mouth and throat region as caused for instance by fresh fruits, vegetables and spices are typical of this type of food allergy. This form of allergy is generally associated with hay fever caused by pollen from trees, grasses and certain weeds. Both pollen and the foodstuffs concerned contain similar proteins that cause the allergic reaction. This phenomenon is called allergenic cross-reactivity. OAS can also occur as a response to true food allergens as in the case of groundnut (De Leon *et al.*, 2003).

Coeliac disease

Coeliac disease (CD) is a chronic disorder of the small intestine resulting from a cell-mediated allergy. The intestinal epithelium becomes flattened, leading to poor absorption of nutrients. The clinical spectrum varies widely and includes abdominal pain, diarrhoea, mal-absorption and poor growth. CD can lead to more serious complications, like osteoporosis, infertility, miscarriage, low birth weight of children born to

mothers suffering from CD, non-Hodgkin's lymphoma and dermatitis herpetiformis. The factors that determine or influence this extremely heterogeneous phenotype are unknown. CD is caused by an inflammatory T-cell response to gluten, a ubiquitous family of dietary proteins from wheat, barley and rye. Gluten molecules are degraded in the intestine and the breakdown products can then set off a cascade of reactions that result in an inflammatory response causing flattening of the villi in the small intestine (Sollid, 2002). A conservative estimate of the prevalence of CD in Europe and the USA is about 0.5% of the population. Several epidemiological investigations show a highly uniform prevalence of 1 in 130 to 1 in 300 amongst all populations of European descent. Studies have shown that the number of undiagnosed cases in some countries may be over 7 times more than is currently officially recognized (Czismadia *et al.*, 1999). Moreover, the prevalence of CD in non-European populations also seems strongly underestimated. It is generally accepted that CD affects people of all racial origins and even in those clinically silent cases of CD, significant nutritional deficiencies may occur and go unrecognized. Early diagnosis will considerably reduce the risk of development of CD-associated diseases such as those listed above. Presenting CD symptoms appears to be modified by factors like dietary gluten load and the age at which an individual is first exposed to gluten.

Increase of allergy occurrence

Although the genetic predisposition to atopy and atopy-related allergies is considerable and possibly still increasing, it cannot explain the extensive enhanced prevalence of allergy, which has doubled in the last decades to up to 25% of the population in western society and still seems to be rising. The increase has often been explained by a decline in infection during childhood through increased hygiene, vaccinations and the application of antibiotics. Other explanations refer to the general increase in smoking, especially in women during pregnancy. The increase has also been suggested to result from reduced incidence of breast feeding and from changes in general eating habits (e.g. the increased consumption of exotic food products).

Recently, much attention has been paid to the 'hygiene hypothesis' to explain the increase in allergy incidence. This hypothesis refers to the balance between various cell types that form part of the immune system. Such a balance is the rule in healthy individuals. However, in allergy sufferers this balance is disturbed. The basis of this disturbance may be found in the loss of control of regulation in the various subsets of cells (called T-cells) that are involved in the immune system. At present, three types of T-cells have been distinguished: the T helper cells (Th1 and Th2), and the T regulator cells (Treg cells). In the case of poor hygiene in combination with a high pathogen load, including e.g. viruses, bacteria, protozoa or helminths, all three types of T-cells will develop, with the Treg cells in a crucial role. So in the case of a high pathogen load, a strong anti-inflammatory network is formed controlling both Th1 and Th2 cells. In the case of limited contact with pathogens, Treg cells are absent, resulting in uncontrolled Th1 or Th2 responses, including the increased occurrence of autoimmune diseases (Th1 related diseases, like diabetes Type 1, rheumatoid arthritis,

multiple sclerosis) and allergies (Th2 related diseases) (Stolte *et al.*, 2002; Yazdanbakhsh *et al.*, 2002).

The patients' point of view

The most common examples of IgE-mediated responses are rhinitis, asthma, eczema and food allergies.

Allergic rhinitis may be chronic or recurrent, and can occur seasonally or continuously. Since the beginning of the 20th century the frequency of hay fever has increased from 1% to an overall prevalence in the general population of about 15–20% today. In many patients suffering from hay fever, the oral allergy syndrome (OAS) will also develop after eating fresh fruits and vegetables due to IgE-mediated cross-reactivity resulting from similar proteins being present in both foods and pollen. A clear example is allergy to apple (and other fruits from the Rosaceae family) and to vegetables from the Umbelliferae family (e.g. celery). These allergies arise from the presence of proteins in these foods that are homologous to the major allergen in birch pollen (Bet v 1) (Breiteneder & Ebner, 2000; Mills *et al.*, 2003).

Allergic rhinitis is under-diagnosed and thus under-treated. It is also considered to be a trigger for the development of allergic asthma. In the 1980s the prevalence of asthma has approximately doubled. A high prevalence occurs during the first years of childhood but there is also a tendency towards increasing prevalence with growth into adulthood.

During recent decades atopic dermatitis (eczema) has increased considerably especially in children under the age of seven. In some populations the prevalence among children can reach levels of almost 25%. These children are at high risk of developing respiratory symptoms in later years. There is convincing evidence suggesting that atopic dermatitis will specifically become a major health problem for individuals born after 1980.

As for food, there is increasing public awareness that many foods cause allergy. Examination of patients shows that about 1–2% of adults, and 6–8% of children suffer from true food allergy. The major foods that cause allergies worldwide are cow's milk, chicken eggs, soya beans, nuts (especially groundnut), wheat, fish and shellfish. In Europe, the relevance of soya beans and wheat to IgE-mediated food allergies is not yet well established. True food allergy is often confused with different forms of food intolerance or sensitivity. Some food sensitivities result indirectly from disorders of the digestive tract or from medical drug treatment. Other food sensitivities result from toxic compounds in the food. In general, it is estimated that roughly 20% of all adverse reactions to food are caused by true immuno-pathologic food allergy.

The impact of having an allergy on the quality of life is considerable. Especially food allergy can isolate people as the patient must avoid eating foods that contain the allergens. In daily practice this can create various problems. Children's parties, outdoor eating and many social activities related to work make it difficult to strictly comply with the dietary rules. Several patients can even suffer from allergies to more than one food. Many common allergenic food ingredients are also present in foods as

hidden components. A clear example is gluten causing coeliac disease (CD). CD can best be treated with a lifelong, strict gluten-free diet. In theory, this means refraining from all foods derived from wheat, rye or barley. However, in practice, this apparently straightforward solution meets with significant difficulties. Most modern foods are processed and even products that appear to be safe to CD patients – such as oats – are actually often unsafe because they are routinely contaminated with gluten from other sources. Sauces, meat products, sweets, mayonnaise, medicinal drugs, coatings, glues, shampoos and other cosmetics, can also contain gluten. Until recently, the ingredient declaration list on food products did not need to indicate the full composition of complex ingredients if they comprised less than 25% of the product. This 25% rule has now been abolished and has been replaced by new labelling guidelines (Directive 2000/13/EC and amended by Directive 2003/89/EC) (Anon., 2003). This makes it obligatory for all ingredients to be indicated on the label, to ensure that consumers suffering from food allergies are fully informed. Nevertheless, even if a complex product contains gluten at just a fraction of 1%, the food in question must still be avoided by CD sufferers. Such is their sensitivity to gluten. This creates huge problems for such patients when the relevant information on the declaration list is incomplete. Moreover, some ingredient lists now indicate ‘may contain gluten’, ‘may contain nuts’, ‘may contain traces of ...’. Unfortunately, such indications are generally a precautionary measure taken to protect the producer but give rise to uncertainty in patients who are allergic, and consequently these products are also avoided even though they may actually be safe.

Other food allergies (e.g. to groundnut, hazelnut, shellfish) can be extremely serious and can cause a life-threatening anaphylactic shock that may lead to a significant fear of food with psychologically aberrant behaviour as a result. This may occur in adult patients, in parents of food-allergic children and even in the children themselves. The effect of ‘eating differently’ may also create psychological problems, especially in young adolescents who are afraid to loose contact with or to become alienated from their peer group.

A different problem relates to diagnosis. Timely diagnosis will prevent the occurrence of many physical and psychological problems. This becomes especially clear in the case of CD, which can result in various vague but serious complaints that are often not immediately recognized as being caused by this disease. Many examples are known of patients who have only been diagnosed in later life and who became symptom-free when using a gluten-free diet, but till then had been living a life of considerably reduced quality.

The economics of allergy

Preventive care is considered a key factor in realizing health benefits. Prevention of allergy in early childhood may provide a good possibility to reduce the ‘allergic march’, i.e., the development of allergy in further life, in two possible ways: extension of sensitivity towards other allergens, and intensifying symptoms. Consequently, the main focus in allergy prevention should be directed towards young children at risk. Howev-

er, the majority of current national health care programmes is still directed towards medical care instead. Assessment of the major economical, allergy-related aspects for society and individual patients takes account of the costs of medical care. An additional economic factor is the size and potential of the markets for medical and dietary products. But this aspect will not be elaborated here.

Searching current literature reveals that little attention has been paid to the true economic consequences of allergies. This is all the more remarkable since about 25% of the European population suffers from some form of allergy. One of the few reliable sources is the European Allergy White Paper (Anon., 1997; 1999). At the macro-economic level, both direct and indirect costs have been distinguished. Direct costs are the travel and treatment costs made by patients visiting and being treated by GP's and hospital specialists, as well as the cost of medicines. Such costs are reasonably well quantifiable. Indirect costs, which are much less easily quantifiable, include e.g. reduced productivity of less healthy workers, extra sick-days and increased time needed for shopping. Direct plus indirect annual costs have been estimated for Western Europe to be about 45 billion € (price level 2004) (Anon., 1997; 1999). Correspondingly, these annual costs are about 2 billion € for a small country like the Netherlands. The direct costs also include, amongst other, the costs of specific dietary products. But not included are the costs that allergy patients are faced with because they often require more expensive or more specialized products that are not designated as dietary and thus are not covered by health care insurance.

Genetic predisposition is a relevant factor in allergy. Children from parents with allergy have an increased risk of becoming allergic too. For this reason the 'Voedingscentrum' (Centre for Human Nutrition) in the Netherlands has proclaimed the 'National standard', indicating that children (babies) who are at risk on the basis of family history, become eligible for preventive measures. This concerns 10–15% of Dutch new-borns. Mother's milk for six months is generally the most obvious food for such babies but in specific cases, however, breast-feeding is not possible, and bottle-feeding is necessary. In such cases, bottle-feed based on hypoallergenic protein hydrolysate is advised. The additional costs of this hypoallergenic bottle-feed are 50%. Currently, the Dutch market for hypoallergenic bottle-feed is only 3%, whereas this market is much larger in neighbouring countries.

Another example relates to CD. The total additional costs of gluten-free food products for diagnosed CD patients in the Netherlands have been estimated at 9 million € annually, or € 1200 per patient per year (Netherlands Coeliac Disease Society; personal communication). However, since only 10% of the total Dutch CD patient population has been diagnosed, these costs comprise a potential annual market for gluten-free food products of 90 million €. Worldwide this amounts to 3.5–4 billion € for gluten-free dietary products alone.

As mentioned above, because of under-diagnosis, misdiagnosis and untimely late diagnosis of allergy, physical and psychological problems will cause a variety of direct medical (e.g. hospital uptake) and indirect societal (non-attendance at school and at work) costs. The costs of medicines to treat allergies are reimbursed by health care insurance companies, whereas the additional costs for hypoallergenic (bottle) food and gluten-free food products – being the only remedy to cure CD patients – are not and

have to be paid by the patient. This situation is different in EU countries like the UK, France, Italy, Greece, Ireland and Sweden, where patients are reimbursed to compensate for the additional costs. Next to a role of the national government, e.g. concerning reimbursements for dietary products, there is also a significant societal role for the food industry in giving a much higher priority to allergy prevention.

Research on allergy prevention

The complexity of the allergy problem has been recognized in the Netherlands and recently the Board of Directors of Wageningen University and Research Centre (WUR) funded an extensive multidisciplinary research programme on various areas related to allergy prevention. Allergy prevention can take place at various levels. In the pre-medical phase the focus is directed towards prevention of sensitization. Secondary prevention aims to stop further progression of the hypersensitivity through avoidance of contact with the allergen and changing the patient's life style. In the medical phase, tertiary prevention is directed towards symptom fighting. In Wageningen most attention is being focused on allergy prevention in the pre-medical phase. Plant Research International already ran a programme on apple allergy, funded by the Dutch Ministry of Agriculture, Nature and Food Quality. This project ran parallel to an extensive EU project on allergies to fresh fruits and vegetables (Gilissen, 2001). This research is aimed at secondary prevention, i.e., development of strategies to reduce the incidence of these types of allergy. Apple allergy develops in north-west Europe in individuals that already suffer from hay fever caused by birch pollen. One of the proteins in this pollen (Bet v 1) causes sensitization in susceptible individuals. Due to cross-reactivity with similar proteins present in fresh food products like apple, cherry, hazelnut and celery, these individuals become allergic and present oral allergy syndrome symptoms (OAS). The relevant protein in apple is called Mal d 1, which is the major apple allergen. Further research concerns (1) the selection of low-allergenic apple cultivars, (2) the localization of the genes for Mal d 1 (and other apple allergens; Gao *et al.*, unpublished results; Gao *et al.*, 2005) on the molecular genetic map of apple, and (3) the knock-out of the expression of the Mal d 1 gene (Gilissen *et al.*, 2005). In addition, Plant Research International has a second research line directed to wheat gluten and CD.

Currently, governmental policy places much emphasis on health, food safety and quality of life in response to major societal developments and needs. Wageningen University and Research Centre has taken up this point and has enabled the establishment of a unique infrastructure, the Allergy Consortium Wageningen (ACW) as a virtual expertise centre with a major focus on research and education on allergy prevention. The five Wageningen Science Groups (focusing on plant, animal, food technology, green environment and societal research) are involved. This enables a strong integration and co-ordination of both research and education. Five research fields have been identified that will be covered by integrated research activities, each steered by at least two Science Groups. Existing collaborations with medical institutions (University Medical Centre-Utrecht, Leiden-University Medical Centre, Sanquin

Blood Supply, and various hospitals and medical laboratories) will be further extended within ACW. Five research fields have been identified and for each a PhD student started in 2004. The research fields are:

1. Allergens in the green environment;
2. Stability of allergens in the food production chain;
3. Consumption patterns and the development of food allergy;
4. Wheat gluten and coeliac disease;
5. Novel foods and allergy concerns.

Allergens in the green environment

Allergens in the green environment, or aeroallergens, are proteins that result in respiratory complaints. About 10% of the population in north-west Europe suffers from hay fever due to sensitization to pollen from birch and related tree species (Fagales). This disease may develop into asthma and – because of cross-reactivity – the occurrence of food allergy to fresh fruits and vegetables is a commonly related phenomenon. An inventory will be made of the distribution of Fagales species in the Netherlands and in the rest of Europe through molecular and genomics approaches with a focus on differences in allergenicity. The objective is identification or production – through genetic modification techniques – of hypoallergenic genotypes for planting in the urban environment. The societal component of this study involves the human attitude towards plantations of genetically modified trees with beneficial characteristics, and the development of an advisory strategy for local and national governments on urban design of the green environment.

Stability of allergens in the food production chain

A ubiquitous group of plant allergens belongs to the so-called Pathogenesis-Related (PR)-proteins. Although these allergens bear many structural resemblances, they behave differently in the food production chain. In particular, some appear to be very stable and are therefore difficult to eliminate through processing. The objectives of this research project is to identify the relationship between the molecular structure of a number of Bet v 1 analogues from different fruit and vegetable species, to study their stability in the food production chain, especially during the various steps of food processing, and to investigate their possible allergenicity. The stability will be measured using both cellular and immunological techniques.

Consumption patterns and the development of food allergy

Allergies originate from interactions between the genetic background of the individual and environmental factors. Allergic sensitization generally occurs at a young age, but the disease can last a lifetime showing phase-wise changes in disease expression and severity. In this project, a study will be made of the indicative and predictive value of immuno-pathological markers obtained from human genomics information. The focus will be on hay fever. A survey will be made of environmental, lifestyle and food intake

variables to develop effective coping strategies applicable to the prevention of hay fever. In addition, the economic impact of hay fever will be analysed.

Wheat gluten and coeliac disease

Up to the present, elimination of gluten intake is the only option to prevent coeliac disease (CD). However, not all gluten proteins and wheat cultivars appear to be equally toxic. This creates possibilities to eliminate toxic gluten from wheat while maintaining its necessary industrial qualities. To this end a genomics approach will be used. Gluten genes form a large gene family. These genes and their alleles will be isolated and sequenced from diploid (ancestral species), tetraploid (pasta wheats) and hexaploid (bread wheats) genotypes. The proteins coded by these genes will then be used to study their toxicity. In addition, the toxicity profile of individual wheat species and cultivars will be examined. The ultimate goal of this research programme is the improvement of the 'quality of life' of CD patients by enabling the development of novel low-toxic wheat cultivars and food products.

Novel foods and allergy concerns

Modified eating habits, resulting in the introduction of new allergens into the daily diet, have been identified as one of the causes of the increase in occurrence of allergy during the last decades. Relevant EU-regulation is being developed to control the safety of novel foods. Testing the presence of allergens is relatively easy in genetically modified (GM) novel foods, but is much more difficult in novel non-GM foods (like exotic fruits, nuts and vegetables). This project involves research on the societal impact of the introduction into the western diet of new products containing potential allergens. Furthermore, the consumer's perception of the acceptability of various scientific and technological approaches to reduce food allergy will be studied. Such a study will be carried out using patient and non-patient groups and will be supplemented with stakeholder analysis. Retrospective (kiwi allergy) and prospective (GM StarlinkTM maize) studies on historical, social, clinical, legal and communicational aspects will be analysed in order to enable the development of allergy prevention strategies in food production chain management. Government and the food industry are the main target stakeholders to advise about the outcomes of this programme.

Discussions on statements

A number of (provocative) statements were made during the recent workshop and presented for discussion. A brief summary of these statements and the responses from the different attendee groups is given below.

Statement 1. *Allergy is a prosperity-related disease.*

Some participants ascribed the increase of allergy during the last decades to improved

diagnostics and to the obvious decrease in child death from other diseases. Others strongly opposed this opinion and stated that the increase of allergy has been demonstrated on the basis of solid scientific data. Solutions for allergy prevention should be searched for in better modulation of the immune system, changing food consumption patterns and changing life styles, rather than in reducing prosperity or omitting vaccination of children. The composition of the intestinal flora may strongly influence the immuno-regulatory network in the human body. Changing food consumption pattern also appears to change the intestinal flora. Other treatments for tertiary prevention include medical therapies like vaccination with allergens (hyposensitization), anti IgE therapies, and the application of cytokine inhibitors. There was no unanimity on a medical approach in the audience.

Statement 2. Prevention at the start of the health care chain will yield the largest health profits/benefits.

Everybody agreed on this statement. However, in practice, only 2% of governmental health care funds is dedicated to allergy prevention whereas 98% is spent on treatment. Diagnosis and cure continue to have highest priority. Primary and secondary prevention are nevertheless considered as being most relevant. Avoiding contact with allergens prevents sensitization as well as further development of the allergic disease, especially in babies. It was proposed that the focus should even be directed towards prevention of contact *in utero*. Saving children from allergy will increase their quality of life considerably. In the future, the possible development of gene passports may be helpful in identifying the type of allergy an embryo or young baby may become susceptible to. At that early age, a primary prevention programme could then be initiated. If necessary, after maturation of the immune system, the child can be hyposensitized using vaccination with the relevant allergen(s).

Statement 3. Birch pollen is the main cause of hay fever, allergic asthma and several pollen-related food allergies; in the Netherlands, all birch trees should therefore be eliminated from the urban environment.

Some participants agreed with comments like: “the best birch is a plastic birch”, while others disagreed because birch is endemic and impossible to eradicate. It is unclear whether patients suffer from the pollen of the birch tree in their garden or from pollen that hails from a much greater distance, e.g. Scandinavia. Analogous to an increase of cypress allergy as the result of increasing cypress planting in gardens, the impact of the garden birch is considered to be significant. Discussion demonstrated the need for improved communication between scientists and responsible local and national authorities. Prevention might be assisted by planting birch cultivars that are selected as being hypoallergenic or male sterile (natural non-pollen producers, or developed through genetic modification).

Statement 4. The niche market for hypoallergenic products is too small and too fragmentary for diet food producers to get any return on investment.

The food industry agreed with this statement. If a food company plays a major role in the food market, it is felt as a commitment to their clients that it should also produce dietary products. This makes the development of hypoallergenic food products industry-driven and fragments the market. On the other hand, offering food specialities, just like hypoallergenic products, may distinguish the various players in the market. Although hypoallergenic foods touch a public health problem, and the production of such foods might be government-driven, so far stimulation from government is minimal. Furthermore, there remains the fundamental desire from industry for research on whether prevention of the presence of allergens in baby foods may also inhibit the development of allergies in later life. A different item relates to the current food products that are becoming more and more unreliable for allergic patients due to the use of a myriad of supplements and additives, which hampers the purchase of foods that are safe for allergy sufferers. An example is the coating of potato chips with gluten to stick on the paprika powder flavouring. In general, such cases can result in 'may contain' labelling by companies of such products, to avoid damage claims. To improve this situation, a re-evaluation of the production chain of complex food products is needed, starting at the level of primary production, including the processing steps and ending in clear labelling to inform the consumer. However, this inevitably will increase the price of these products.

Statements 5 and 6. *Allergy is a medical rather than an agricultural problem, and The interest of politicians in allergy and allergy prevention has to increase enormously in the coming years.*

These statements were taken together. The common feeling was that allergy is not only a medical problem, but strongly links agriculture, food production and processing, the living environment and health. Integrated research across these fields is essential. The approach of the Allergy Consortium Wageningen is a good example that deserves strong support. In addition, a proposed 'Ministry of Research' would be a solution to establish more easily cross-links between the relevant parties.

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