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Review

Novel foods and food allergies: A review of the issues

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This review identifies and explores the current issues around different types of novel foods and allergy concerns. An important issue relates to the observation that risk estimates associated with novel foods may differ depending on whether more emphasis is placed by the individual on the results of technical risk assessment or on an individual's perceptions of risk associated with different hazards. Consumer perceptions of benefits associated with novel foods also vary. Perceptions of what constitutes both risk and benefit appear to be important determinants of consumer acceptability of particular products. One conclusion that can be made is that novel foods have the potential to contribute to food allergy management, but that consumer acceptance is likely to differ according to the preferences of individual consumers. It is concluded that some novel foods may result in improvements on the quality of life of food allergic patients, whereas others may result in the development of further socio-economic problems.

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Introduction

This review aims to identify and explore issues around novel foods and food allergies. A food allergy is defined as an aberrant fast immunological reaction to normally harmless food components, usually proteins (Sampson, 1999a). Food allergy is distinguished from food intolerance, which is a non-immune-mediated reaction. In contrast with food allergy, symptoms of food intolerance can take several days to manifest themselves. Novel foods are defined as foods or food ingredients that have no history of safe use in the European Union (EU). The absence of a history of safe use can be the result of: (1) genetic modification of the food or production of the food using genetically modified organisms, (2) novel processing techniques, or (3) the food being new to the European Union. That is, although the food has a history of use in other parts of the world, this is not the case in Europe. The latter category is in the context of this paper referred to as novel imported foods.

There is some evidence that food allergy prevalence is increasing in some parts of the world, although this is not definitively proven (Helm & Burks, 2000). One aspect of food allergy that needs further consideration is that of novel foods. The introduction of novel proteins into the food chain and the human diet may result in new cases of food allergy. In contrast, the elimination of allergenic proteins may lead to reduced risk of allergy. In both cases, consumer and other stakeholder attitudes towards the application of novel technologies to food production complicate the issue of commercialisation of novel foods. For the purpose of this paper we will consider food allergy and novel foods in the context of the European Union. However, the issues discussed are generic and have international applicability.

Various organisations and individuals have an interest in the issue of food allergy. Examples of stakeholder groups are food allergic individuals and their families, health professionals, the food industry, policy makers, public health authorities, non-governmental organisations (NGOs), patient organisations, scientists and finally the general

public, who may have to deal with the issues associated with food allergy on an occasional basis.

This review paper will discuss the different risks and benefits associated with novel foods within the context of technical risk assessment, as well as public risk perceptions regarding the acceptability of different kinds of novel foods. We will then discuss food allergy prevalence, which may be on the increase, although the literature is varying regarding this issue. Quality of life may be negatively affected by food allergy (Sicherer, Noone, & Muñoz-Furlong, 2001) and also needs to be addressed. In addition, different strategies for allergy management and the role novel foods can play in the development and enactment of allergy management will be discussed. Finally, future research needs will be identified.

Novel foods

Novel foods may be introduced into the food chain in order to attain some associated potential societal or environmental benefits, (Rowland, 2002) but may also be associated with some (perceived) risks (Shewry, Tatham, & Halford, 2000). We provide an overview of the risks and benefits associated with novel foods, as both these factors are likely to influence the acceptance of novel foods by consumers.

Risks and benefits

Genetically modified foods

There is an extensive literature regarding consumer attitudes to the introduction of genetically modified foods, particularly in Europe (Frewer *et al*., 2004). Various factors determine consumer acceptance of genetically modified foods, including those relating to perceptions of involuntariness of exposure regarding individual consumption, inability to trace genetically modified foods and ingredients in the food chain, and perceived unnaturalness of food products and production methods. In the area of health, many consumer concerns about genetically modified foods are related to the uncertainty of the (potentially long term) effects on consumer health in general (Frewer & Salter, 2003; Miles & Frewer, 2001) including increased allergenicity associated with the introduction of novel proteins into the human food chain (Shewry *et al*., 2000). An example of this is the 2S albumin in the Brazil nut which was used in transgenic soy bean, to which some consumers are allergic.

Although the process of genetic modification may introduce new allergenic proteins into foods, it can also be used to remove established allergens (Kuiper, Noteborn, Kok, & Kleter, 2002; Shewry *et al*., 2000). At the present time, it is unknown whether food allergic consumers would be willing to buy and use these hypoallergenic foods, or whether allergic consumer acceptance would be contingent on the severity of the allergic reaction experienced (Schenk *et al*., in preparation).

Benefits associated with genetically modified novel foods include improved yield, enhanced plant disease resistance, improved taste and other quality parameters, and improved growth in adverse conditions such as drought and low temperatures (Rowland, 2002). Many of these benefits are similar to those that have been achieved in conventional breeding programs. However, whereas some traditional breeding techniques aim at changing as many genes as possible in the plant genotype in order to produce the desired changes, genetic modification permits the expression of the target gene(s) alone.

Consumer's perceptions of the risks and benefits of genetically modified foods influence acceptance or rejection of specific products. Miles and Frewer (2001) have demonstrated that the extent of the accrual of benefits, and to whom these benefits accrue, (for example, to industry or consumers) appears to be an important factor in consumer acceptance. To date, most of the advantages conferred by genetic modification in the agrifood sector are linked to improvements in agronomic traits, which have no direct benefit for consumers. Thus, if we assume that consumer acceptance of genetically modified foods is underpinned by consumer recognition that there are direct benefits to consumers, it is unlikely that improvement in agronomic traits alone will result in consumer approval of novel products (Frewer, Scholderer, & Bredahl, 2003; Miles & Frewer, 2001; Saba, Moles, & Frewer, 1998).

Genetic modification of crops may result in novel foods with improved quality characteristics, improved nutritional and health attributes, resistance to spoilage and even reduced levels of allergens, which have a direct benefit for consumers (Kuiper *et al*., 2002; Taylor & Hefle, 2001). Research by Saba *et al*. (1998) indicates that some consumers would be willing to buy genetically modified foods with consumer oriented benefits. However, at the present time, more research is needed to clarify whether consumers would be willing to buy genetically modified foods with benefits in terms of reduced allergenicity.

Foods produced using other novel processing techniques

Examples of processing techniques that are at the time of writing, considered 'novel' are thermal processing, high-pressure processing, ultra filtration and γ-irradiation. All of these techniques have been introduced in order to improve food safety and quality. Application of these techniques may reduce or increase allergenicity (Davis, Smales, & James, 2001). For example, the impact of thermal processing on the presence of food allergens depends on which specific allergens are present in the food. The major apple allergen, Mal d 1, is a protein that degenerates easily following thermal processing. This denaturation changes the structure of the protein, which makes it impossible to be recognised by immunoglobulin-E (IgE). As a consequence, the consumer does not suffer from an allergic reaction to the protein. In contrast, some fish allergens do not produce an adverse reaction when the product is fresh, but produce an allergic response after these are cooked (Davis *et al*., 2001; Wigotzki, 2001). Further analysis is required to determine systematically which allergens are activated and which ones

are eliminated during various methods of novel processing. The benefits of novel processing techniques include increasing the shelf life of products without negatively altering structure and taste.

Novel imported foods

The major risk associated with novel imported foods is that they contain proteins that may provoke allergic reactions within populations where they have been newly introduced into the diet. This increased risk is the result of globalisation and increased allergen distribution through the world. Related to this is the risk that the new proteins are cross-related to known allergens, or those which are already extant in a particular food chain. The major benefit of novel imported foods is the increased diversity of food from which consumers can choose and possibly as a consequence, the increase of healthy compounds in the diet (Bäckström, Pirttilä-Backman, & Tuorila, 2003).

Risk conflict

Different individuals appear to evaluate the risks and benefits of novel foods in different ways, and this also varies across different applications. Very broadly, it appears that there are differences between the way that experts and non-experts evaluate risks, an observation established over many different types of hazard (Slovic, 1999). In the present discussion, we refer to this difference as risk conflict.

Technical risk assessments are frequently the basis of risk management practices within the risk analysis framework. Technical risk assessments are often used by experts and regulators to determine acceptable safety levels (Taylor & Helfe, 2001), although consumer decision-making is, in part, based on broader, societally relevant factors of concern (Frewer *et al*., 2004). The latter will be discussed in Section 2.2.1. Assessment of potential allergenicity is, of course, only one component of the risk assessment of novel foods (Kuiper *et al*., 2002; Rowland, 2002). Microbiological and toxicological risks are also important, although they are not relevant to the topic of allergenicity.

Consumer risk perceptions

Risk perceptions are a specific form of attitude towards a particular object, such as a potential food hazard (Frewer *et al*., 2004). These include factors such as the extent to which an individual perceives the risk of a hazard to be uncertain, dreaded, potentially catastrophic, uncontrollable, equitably distributed and presenting risks to future generations and influence people's acceptance of a particular hazard (Slovic, 1999). This broad concept of risk implies that psychological responses to a particular hazard may not directly relate to technical risk estimates resulting from a formal risk assessment procedure. In contrast, experts tend to see risk as synonymous with probability of harm, or expected mortality, consistent with the way in which risk tends to be characterised in risk assessment. Therefore, technical risk estimates, traditionally provided by experts, influence people's behaviours in a different way than risk perceptions (Frewer *et al*., 2004). As a result, many conflicts over the risk of foods may result from different stakeholders having different perspectives (Slovic, 1999). For example, in the case of Starlink maize, most experts estimated the chance of Starlink provoking an allergic reaction in human consumers to be very small. Despite these reassurances from the expert community, the discovery of Starlink maize in tacos destined for human consumption was viewed negatively by the consumer, and consequently resulted in the recall of almost 300 maize products (Gremmen *et al*., 2004).

People's responses to risk are psychological, such that people's perceptions about a particular hazard influence their responses to it (Frewer *et al*., 2004). The social context of risk also plays an important role in how people represent risk (Joffe, 2003). Social representation theory can provide a useful framework for examining risk perceptions of novel foods and the way science enters the domain of everyday thinking (Bäckström *et al*., 2003). Social representations can be defined as systems of relevant values, ideas and practices (Moscovici, 2001), and can be used for research focussed on the social construction of social knowledge (Flick, Fischer, Schwartz, & Walter, 2002). Bäckström *et al*. (2003) have demonstrated using social representation theory that the risk perceptions associated with novel foods are multidimensional. In other words, people make sense of unfamiliar novel foods using various dichotomies, such as trust/distrust, safe/unsafe, natural/artificial, pleasure/necessity and past/present. The artificial and unnatural nature of foods produced using genetic modification has been identified as an important dimension for consumer negativity towards these products (Bäckström *et al*., 2003). Trust in science and regulators, or a lack of it has been identified as a potentially important determinant of consumer acceptance of novel foods (Frewer *et al*., 2003).

Genetically modified novel foods

Governmental regulatory agencies in most developed countries require a mandatory safety assessment and consultation with governmental regulators before commercial sale of genetically modified foods is permitted (Taylor & Helfe, 2001). However, the assessment process applied to determine the allergenic potential of genetically modified foods presents major problems, since there are no reliable tests for predicting clinical allergenicity. As a consequence, assessment of allergenic potential has often focused on determining whether the novel product is substantially equivalent to the traditional counterpart (Taylor & Helfe, 2001). The safety of traditional foods and ingredients is usually accepted on the basis of their history of safe use. As a consequence, there is general consensus that, where possible, safety assessment should use traditional foods and ingredients as reference points, and that assessment processes should focus on the differences between these traditional foods, and the novel foods and ingredients under assessment (Howlett *et al*., 2003). If a novel food is determined to be substantially equivalent, then it is judged to be as safe as its traditional counterpart. If the novel food is

not substantially equivalent it needs to be subject to a broader analysis on a case-by-case basis, with the safety assessment focussing on established differences between the novel food and its conventional counterpart (Taylor & Helfe, 2001). An established decision-tree approach for predicting the potential allergenicity of novel proteins is that of the Codex Alimentarius (2003) and the Food and Agriculture Organisation/World Health Organisation consultation group (2001). This decision tree approach, which assumes that the amino acid sequence is known, is discussed frequently in the existing literature (for example, see Taylor and Helfe, 2001).

Applying this approach provides reasonable assurance that the newly introduced protein has limited capability to develop into an allergen (Taylor & Helfe, 2001). However, it is important to realise that absolute safety is not an achievable standard, since all technologies hold known and unknown risks (Garza & Stover, 2003). This uncertainty is one of the risks frequently mentioned by consumers (Miles & Frewer, 2001).

When during this risk assessment process no particular concern is indicated for any specific population group (not only known food allergic individuals), the occurrence of non-immunologically based reactions may still become apparent post-launch. This indicates the need for post-launch monitoring (Howlett *et al*., 2003). It should be noted that application of the substantial equivalence approach does not satisfy consumer concerns associated with the application of genetic modification more generally. For example, a consumer concerned about the potentially negative impact of genetically modified crops on the environment, independent of the absence or otherwise of novel proteins in foods to be consumed, may not be reassured by claims of substantial equivalence of novel foods (Frewer *et al*., 2004).

Foods produced using other novel techniques and ethnic novel foods

It should be noted that expert risk assessment focuses on the novel protein as unit of analysis, rather than the complete food. This is because a few genes are introduced into a particular genome. As a consequence, it remains exactly the same, except for these genes, so it is only necessary to focus on the new protein which results from the inclusion of additional genes (Howlett *et al*., 2003). However, for foods that are produced with the use of novel processing techniques, and for novel imported foods, it is not sufficient to assess whether a single protein has been produced. In the case of various processing techniques it is not effective to assess the amino acid sequence, because in most cases the amino acid sequence does not change. Instead, it is the protein structure that changes and that reveals or hides an epitope, which is the binding site on a protein for IgE.

In the case of novel imported foods it is not possible to focus on a single protein because the product may not have been introduced into a particular food chain before and, in the case of foods introduced into the European market, possess a genome that has not been described previously. It is therefore not possible to examine the amino acid sequence of specific foods, and the decision tree approach cannot be applied to novel imported foods. However, in most of these cases, it is possible to identify an established food that is similar, either in terms of plant function, or because it has a botanical relationship to the novel imported food. It is also possible to screen for known allergenic proteins in the novel imported food. These proteins can be compared to known allergenic proteins. This means that it is possible to use the substantial equivalence principle, and as a result the novel imported food is considered safe if the comparable counterpart has a history of safety (Howlett *et al*., 2003; Kuiper *et al*., 2002).

Of course, it is arguable that experts also apply factors other than those grounded in rationality (Jensen & Sandøe, 2002). Thus it is important to acknowledge that experts apply values to risk assessment, and lay people are capable of reasoning. However, experts tend to utilise arguments originating in technical risk assessment to a greater extent than do the public in proposing different arguments about risks of novel foods (Gremmen *et al*., 2004).

Novel food acceptance

In the area of (food) technology innovation, people may tolerate some level of risk associated with (for example) production processes if they also perceive direct benefit to themselves as consumers, rather than to other groups in society, such as producers or the food industry (Frewer, 2003). Scientists and industrialists have, in the past, assumed that consumers will accept novel products with a specific consumer benefit. However, just as the public, to some extent, defines risk in a different way to experts, (Van Kleef *et al*., submitted for publication) it is possible that the public also defines benefits differently. In addition, what is perceived to be a benefit associated with a novel food differs between different countries and cultures, and between different individuals at different times and within different contexts (Frewer *et al*., 2004). Genetically modified foods with reduced or absent allergenicity may be perceived as highly beneficial by food allergic consumers and thus acceptable. For non-allergic consumers, the perceived risks may outweigh the benefits. It might be concluded that, as long as risk is not so large as to be completely intolerable, an individual's acceptance will be driven by perceptions of personal benefit (Frewer, 2003). However, individual differences in attitude, in part shaped by personal needs and requirements also need to be taken into account. We can explain the relative acceptability of novel imported foods when compared to genetically modified foods. The introduction of novel foods from different cultures, may be accepted by a particular group of consumers more easily because they have already been 'tested' by other people (Bäckström *et al*., 2003), or because they are considered to be natural in origin, and thus tolerable.

There is thus some theoretical evidence regarding the factors which may influence consumer acceptance of novel foods, at least in Europe. It remains unclear, however, whether consumers will accept novel foods in practice. Technical risk assessment processes currently used by risk assessors and regulators is only of partial utility in developing a risk communication strategy, as it does not address some important consumer concerns.

Food allergy and society

It is said that the prevalence of food allergy is increasing (Helm & Burks, 2000). In order to assess the extent of the food allergy problem it is important to understand the reported prevalence of food allergies.

Food allergy prevalence

Although the increasing prevalence of food allergy is frequently mentioned in the food allergy literature, information regarding formal assessment of the epidemiology of food allergy is less often presented (Altman & Chiaramonte, 1996; Crevel, 2002; Fraser, Sumar, & Sumar, 2000; Helm & Burks, 2000; Kagan, 2003; Kimber & Dearman, 2002; Oehlschlager *et al*., 2001; Thompson & Chandra, 2002; Zeiger, 2003). Only a few articles have reported primary data on food allergy prevalence (Eigenmann, Sicherer, Borkowski, Cohen, & Sampson, 1998; Sicherer, Muñoz-Furlong, Burks, & Sampson, 1999; Sicherer, Muñoz-Furlong, & Sampson, 2003; Woods, Abramson, Bailey, & Walters, 2001). At the present time, it is not understood whether the introduction of novel foods will contribute to an increase in food allergies, or if genetically modified novel foods with reduced allergenicity will significantly reduce food allergy prevalence. This requires close monitoring in the future.

Table 1 gives an overview of food allergy prevalence for both children and adults reported in different literature sources. One distinction that is made in this table is between the prevalence of 'true' food allergy and 'perceived' food allergy. True food allergy prevalence refers to the percentage of patients in a population with a formal diagnosis of food allergy. Perceived food allergy prevalence refers to the people's belief that they personally exhibit the symptoms of a food allergy, independent of whether a health professional would diagnose them as food allergic. This means that the self-reported data leading to population level estimates of prevalence of perceived food allergy may include both food allergy and food intolerance and maybe even other adverse reactions to food. This explains why the public's perception of food allergy prevalence may be much higher than is supported by the actual prevalence data. The data summarised in Table 1 show that there is no agreement within the existing literature regarding the prevalence of food allergy. One of the reasons for this lack of agreement is that it is difficult to diagnose food allergy. The Double-Blind-Placebo-Controlled Food Challenge (DBPCFC) is both expensive and time consuming for patient and doctor. Other diagnosis methods are Radioallergosorbent tests (RAST) in which the amount of specific IgE is tested, and skin prick tests (SPT) where glycerinated diluted food extracts are applied to the skin by prick technique (Sampson, 1999b). It is important to note that there are two phases of food allergy: the primary contact with an allergen and the later repetitive contact with an allergen, which results in symptoms (Mills, Madsen, Shewry, & Wichers, 2003). Some individuals become sensitised, but never develop the symptoms. These individuals will get positive results from RAST assays and SPT, but a DBPCFC will give negative results. Diagnosis is therefore highly dependent on the diagnosis method used, which clearly contributes to ambiguities in food allergy prevalence rates. Other diagnosis methods available are questionnaires and self-report data. These are not reliable methods of food allergy diagnosis because food allergy symptoms are often similar to those associated with other adverse reactions to food, (for example nausea), which results in a higher reported food allergy prevalence than actually is the case. Another problem in developing accurate prevalence estimates is that only a few studies analyse food allergy prevalence across complete populations, as opposed to population segments. This is illustrated by the study of Eigenmann *et al*. (1998) who report a food allergy prevalence of 37% in a population of children suffering from atopic dermatitis (Eigenmann *et al*., 1998). Although the prevalence in this population could be accurate, it makes comparison of prevalence rates with other studies and other populations difficult. In addition, there is a lack of uniform definitions of various adverse reactions to food, resulting in problematic interpretation of research findings. The effect of this can be seen in the third column of Table 1 where the definitions of food allergy used in patient diagnosis vary across research studies. There is, however, general agreement that the prevalence of food allergy in children is higher than in adults (Altman & Chiaramonte, 1996; Bock, 1987; Chandra, 1997; Crevel, 2002; Kimber & Dearman, 2002; Sampson, 1999a). The greater prevalence in children can be explained by an increased predisposition of children to develop food allergy, and by the tendency for children to develop immunologic tolerance as they get older.

However, due to the incomparability of the data presented in Table 1 it is not possible to conclude that food allergy prevalence has increased. The only studies that show a small increase in peanut and tree nut allergy prevalence are those of Sicherer *et al*. (1999, 2003) who found a slight increase in prevalence in children of over five years of age. However, there is some indirect evidence that indicates that food allergy prevalence is increasing. The first indication for this increase is cross sensitisation, which means that food allergy often occurs in combination with other allergies. It has been established that the prevalence of

Table 1. Food allergy prevalence

Year[a]	Prevalence	Diagnosis[b]	Food[c]	C/A[d]	Population[e]	Country[f]	Source
1980–1984	28% 8%	Parentally reported FA DBPCFC	No specific foods	C	480 children followed prospectively from birth to their third birthdays	USA	(Bock, 1987)
Before 1988	5.3% 1.7%	Parentally reported FA Open food challenge	No specific foods	C	Infants 0–6 months	The Netherlands	(Douwes, Weert-Waltman van, Folkertsma, Fagel, & Verboom, 1988)
1989–1992	12.4% 2.4%[g]	Self reported food allergy/ food intolerance DBPCFC	No specific foods	A	Healthy Dutch adults 1483 individuals	The Netherlands	(Niestijl Jansen *et al.*, 1994)
1991–1994	12%	Self reported FA/FI	No specific foods	A	Cross sectional sample of 17280 adults aged 20–44 years	14 European countries and USA	(Woods *et al.*, 2001)
Before 1994	1.4–1.8[h]	Self reported FI	No specific foods	A+C	15000 households (7500 cross sectional, 7500 randomly selected nationwide)	UK	(Young, Stoneham, Petruckevitch, Barton, & Rona, 1994)
1997	0.6% 1.6%	Self reported allergy	Peanut or tree nut allergy	C A	4374 households nationwide sample children under 18 years 4374 households nationwide sample	USA	(Sicherer *et al.*, 1999)
Before 1998	37%	IgE (six foods)	Milk, egg, peanut, soy, wheat, fish	C	63 patients with atopic dermatitis between 0.4 and 19.4 years	USA	(Eigenmann *et al.*, 1998)
2002	1.2% 1.3%	Self reported	Peanut or tree nut allergy	C A	4855 households nationwide sample 4855 households nationwide sample	USA	(Sicherer *et al.*, 2003)
2002	0.6% 2.8%	Self reported	Sea food allergy	C A	5529 households nationwide sample 5529 households nationwide sample	USA	(Sicherer, Muñoz-Furlong, & Sampson, 2004)

[a] The year in which the study was conducted.
[b] The diagnosis column refers to the method that was used to diagnose the participants of the study.
[c] In this column is indicated whether the reported prevalence rate applies to a specific type of food.
[d] C and A indicate whether the study was focused on children, adults or on both.
[e] Information about the sample and population the sample was drawn from.
[f] County in which the study has been done.
[g] Estimated, based on Double-blind Placebo-controlled Food Challenge and on the assumption that FA/FI is equal among participant, non-participants and drop-outs.
[h] 1.4% with stringent criteria and 1.8% with less-stringent criteria.

other allergic diseases such as pulmonary or occupational allergies is increasing, which suggests that the prevalence of food allergy might be increasing in line with this general trend (Jansen & Brussaard, 2001). Another indication of increased prevalence is provided by the observation that peanut allergy is becoming more common in younger generations, but not in older ones (Hourihane, Dean, & Warner, 1996). Since peanut allergy is rarely outgrown, it can be expected that peanut allergic children will continue to suffer from peanut allergy as they get older. The third indication is the fact that, as a consequence of the increase of global trade, the variety of food consumed at the present time is higher than in the past. As a result, people will be increasingly exposed to a wider diversity of food antigens, which may result in increased food allergy (Fraser *et al*., 2000; Jansen and Brussaard, 2001).

Socio-economic impact

Food allergies can have a significant impact on the quality of life and economic functioning of people who suffer from them, as well as wider implications for society more generally. The economic impact of food allergy is composed of both direct and indirect costs. Direct costs include both medical and non-medical expenses associated with the disease, such as prevention and treatment costs and transportation costs associated with healthcare provision (Gergen, 2001). Indirect costs are linked to factors such as work and productivity. The introduction of novel foods with reduced allergenicity may be readily accepted if these foods have a positive effect on quality of life and economic functioning. However, it is unlikely that improvements in socio-economic functioning of food allergic patients in isolation of other societal benefits will facilitate global marketing of foods previously confined to specific ethnic groups or geographical locations, because such benefits only apply to a limited number of people. The economic impact of food allergy is difficult to estimate because of a lack of knowledge about the population-level prevalence. In addition, a cost for one stakeholder group may represent a benefit to another stakeholder group. In the case of allergy, for example, medication will result in costs for patients or insurance companies, but generate profits for the pharmaceutical companies. Patients will, of course, also benefit from alleviation of symptoms (Mugford, 2004). In the European White Paper on Allergy (1997) the socio-economic costs of allergy have been estimated. The total costs of the major allergic diseases (including allergic rhinitis, allergic asthma, atopic dermatitis, contact dermatitis and urticaria) are estimated at 10 billion ECU for direct costs and 19 billion ECU for indirect costs. Food allergy is not mentioned as one of the major allergic diseases in this report, perhaps because of the paucity of information available to permit cost estimation regarding direct and indirect costs (Aas *et al*., 1997).

Generally speaking, the costs of food allergy are conceptualised in different ways by different stakeholder groups within society. If the economic costs are assessed by risk regulators and public health authorities, one might expect that both direct and indirect costs are considered important, and thus should be taken into account when implementing a strategy regarding the commercialisation of novel foods, whether from the perspective of allergy reduction, or reducing any potential for increased prevalence of food allergy. From the food manufacturers and retailers point of view, the direct costs tend to carry greater weight, because they tend to influence the cost of business activities. From an industrial perspective, indirect costs are of less importance as quality of life is not a direct issue. The liability of food manufacturers regarding hidden allergens in products is an increasingly relevant issue, as liability claims can have an impact on direct costs of food manufacturers if labelling is inaccurate (Crevel, 2002).

The indirect costs of food allergy have a much greater impact on individuals and families, because these costs reflect the functioning and quality of life of the individual and the family where a family member suffers from a food allergy (Gergen, 2001). The social impact of food allergy primarily relates to potentially negative effects on quality of life (QoL). Food allergy can have a profound impact on quality of life, not only because of the immediate clinical effects related to individual's allergic condition, but also because of the alterations in daily life which are needed in order to prevent the occurrence of food allergy symptoms and the influence on psychosocial functioning of the individual (Sicherer *et al*., 2001). Reactions that can occur when a food allergic individual is exposed to allergens range from abdominal pain, vomiting and/or diarrhoea to cardiovascular symptoms, including hypotension, vascular collapse and cardiac dysrhythmias. Exposure to a food allergen can even result in anaphylaxis, which may be severe enough to be life-threatening (Sampson, 1999a). Thus food allergy may result in restriction of social activities (for example, eating outside the home, more problematic shopping expeditions) and anxiety (Knibb *et al*., 2000). The only reliable therapy used to treat food allergy at the present time is restriction or complete elimination of the responsible food allergen and emergency management of reactions in case a food allergen is accidentally ingested. Needless to say, this has a negative impact on the quality of life of both the food allergic individual and their families (James, 2001), as well as an emotional impact (Meltzer, 2001), and psychological distress (Knibb *et al*., 1999), and restrictions on leisure activities and other lifestyle factors (Knibb *et al*., 2000). Whilst labelling is informative, (Crevel, 2002) and essential for consumers with a diagnosed food allergy (Mills *et al*., 2004), the introduction of novel allergens may result in allergic responses independent of a labelling policy, as individuals will not know to which foods and ingredients they will experience negative reactions.

Management of food allergies

Prevention

An important step of food allergy management is prevention. Zeiger (2003) identifies three phases of prevention, primary, secondary and tertiary. Primary prevention essentially means blocking of immunologic sensitisation and thus reducing the prevalence. Secondary prevention is interpreted as suppression of disease symptoms after immunologic sensitisation has occurred. Tertiary prevention represents the stage in which symptoms are treated and worsening of the patients situation is prevented (Zeiger, 2003).

Primary prevention

Primary prevention appears to be beneficial only for infants with an atopic family history (Zeiger, 2003). A critical time in early infancy can be identified in which the genetically programmed atopic infants are at higher risk to become sensitised to ingested and/or encountered food allergens. Prenatal exposure may also be problematic in terms of sensitisation. Some novel foods can help in primary prevention as they do not expose the child to potential allergens. However, it cannot be assumed that all food allergens are already identified. This means that it may not be possible to avoid the yet unidentified food allergens. This could be the case with novel imported foods, since their amino acid sequence is, in most cases, unknown. In addition, it is difficult to identify in advance which proteins in novel foods could cross-react with known allergens. Predictive testing of food to identify allergens is a method of primary prevention, because it enables risks to be identified, which is the basis for control, but this procedure cannot identify the risk of cross-reactions (Smith, 1997). Thus primary prevention of food allergy should focus not only on food allergens, but also on the avoidance of allergens that are not directly causing food allergy, but might do so due to cross sensitisation, as is the case with birch allergens.

Secondary prevention

Once sensitisation has occurred, avoidance of the food allergens is the only proven strategy to prevent the occurrence of symptoms. Strict elimination diets may lead to malnutrition, especially if they include a large number of foods and/or are used for extended periods of time (Sampson, 1999b). Elimination of a single food can be difficult, especially when the food is used in many other food products, such as milk. Labelling is an important part of secondary prevention because it enables individuals to avoid foods to which they are already hyper-sensitised (Smith, 1997). A prerequisite for this is that the information on the label is readily understood by the consumer (Crevel, 2002).

It should be noted that there is a difference between treatment of a disease and life-long avoidance (Kilshaw, 1981). In case of food allergies, the impact of avoidance on the daily lives of food allergic consumers and their families forms a major part of the socio-economic problems associated with food allergy. Avoidance is therefore not a real solution for the food allergy problem, although it currently is the most important part of food allergy management. Novel foods can help with secondary prevention because their potential for inducing allergic responses may be reduced.

Tertiary prevention

Given the difficulty of avoiding food allergens, it must be assumed that patients may experience accidental ingestion of problematic foods. Contamination with an unrelated food during the manufacturing process or misrepresentation of a food item on a label are common causes of accidental exposure to known allergens (Thompson & Chandra, 2002). Medications, such as anti-histamines, have been used in an attempt to modify symptoms of food-induced allergic disorders, but overall they have minimal efficacy. Oral corticosteroids are generally effective in treating chronic IgE-mediated disorders, but side effects are generally unacceptable to patients (Sampson, 1999b). In case of anaphylaxis, injection of epinephrine is the primary treatment, even in the early stages before the onset of life-threatening symptoms, as treatment failure is more likely if epinephrine is delayed (Thompson & Chandra, 2002). Children with symptomatic food allergy often lose their allergy over time. Exceptions tend to occur in most cases of peanut, tree nut, and seafood allergy (Sampson, 1999b). Consequently, food challenges should be repeated at set intervals to determine whether the dietary restrictions are still necessary (Bruijnzeel-Koomen *et al*., 1995).

Tertiary prevention involves medication of symptoms and therefore it is unlikely that novel foods can play a role in tertiary prevention.

Conclusion

It is obvious that primary prevention, the prevention of sensitisation, is the best strategy to decrease the food allergy prevalence, because this type of prevention reduces the socio-economic impact on the daily lives of food allergic consumers and their families. Secondary prevention does not really prevent allergic disease, but only prevents the occurrence of symptoms. In an ideal situation secondary prevention is not necessary, because primary prevention would have proven to be successful. Given that tertiary prevention is nothing more than treatment of the symptoms, it still represents an important part of food allergy management, as these symptoms can be severe, or even fatal.

Novel foods applied to food allergy management

The incidence of severe (and potentially fatal) food-induced allergic reactions indicates that current management strategies (allergen avoidance and early use of epinephrine) are not adequate for dealing with food allergies (Leung & Bock, 2003), suggesting that additional management strategies are needed. Novel foods may facilitate food allergy management. One approach under investigation involves the mutation of IgE binding epitopes on major peanut proteins. The mutated recombinant protein may desensitise patients with peanut allergy in a manner similar

to standard immunotherapy without the risk of inducing anaphylactic symptoms (Sampson, 1999b). Another approach under investigation involves the development of hypo-allergenic foods. In these foods, most allergens have been removed chemically, enzymatically or by formulating the food product from different ingredients. For example, rice has been genetically modified to suppress the expression of a gene encoding for a certain allergen (Laiho, Ouwehand, Salminen, & Isolauri, 2002). However, it is unlikely that *all* consumers will accept the introduction of genetically modified rice into the food chain, particularly those not suffering from food allergy. However, allergic consumers may be enthusiastic about these novel foods, resulting in the development of niche markets for hypoallergenic food products.

Differences in the neonatal gut micro biota may precede the development of atopy. The modification of the gut micro biota by means of novel foods induces beneficial effects that may reduce the risk of allergic disease (Nowak-Wegrzyn, 2003). Allergic disease could be prevented through nutritional management capable of preventing or depressing allergic inflammation based on the administration of novel foods containing strains of beneficial microbes (Laiho *et al.*, 2002). However, again the issue of product acceptability based on consumer response may need to be addressed.

Conclusions

In this review we have identified various issues surrounding novel foods and food allergy. An important issue is that there are both risks and benefits associated with novel foods. Consumer acceptance of novel foods is contingent on both technical risk estimates, and consumer perceptions of both risk and benefit. Furthermore, consumers are not homogenous, and what is perceived as a desirable benefit by one consumer may be regarded as irrelevant by another. In the case of novel foods, genetic modification directed towards reducing allergenicity may be viewed positively by allergic consumers, but is unlikely to meet with general consumer approval. This suggests that such products should be marketed specifically to consumers who want to buy them, under conditions of fully informed consumer choice.

Consumers perceive ethnic novel foods are less risky than genetically modified foods (Bäckström *et al.*, 2003). However, the example of kiwi fruit proves that novel imported foods cannot be considered safe from an allergy point of view without proper safety analysis (Bublin *et al.*, 2004; Lucas, Grimshaw, Collins, Warner, & Hourihane, 2004).

It can be concluded that novel foods, despite some risks, have the potential to contribute to food allergy management. They can contribute particularly to primary and secondary prevention by avoidance of the concerning allergens. For tertiary prevention, novel foods are less helpful. However, novel foods can also potentially increase the prevalence of food allergy through introduction of novel or unlabelled allergens into the human food chain, and this needs to be carefully assessed. It remains unclear what are the allergy risks for novel foods that are not genetically modified, perhaps indicating the need for implementation of a decision tree similar to that applied to genetically modified novel foods.

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