Food Allergens - Allergic Reation to Food

Last Updated : 30 October 2013

1. Differences between food allergy and food intolerance

For a small percentage of people, specific foods or components of food may cause adverse reactions. These are typically classified as food allergies (i.e. reactions which involve the immune system) or food intolerances (i.e. reactions which do not involve the immune system). Allergen terminology has been published by the World Allergy Organization and is based on terminology originally proposed by the European Academy of Allergy and Clinical Immunology (EAACI).[1,2]

A food allergy occurs when an allergen (i.e. a protein in a food, which in the majority of people will not produce an adverse reaction) sets off a chain of reproducible reactions involving the immune system. The reactions can be either antibody- or cell-mediated. The former is the most common and occurs in two stages[3,4]:

1. **Sensitisation:** Initial contact with an allergen does not evoke an allergic reaction but rather primes the immune system. Dendritic cells (a special type of white blood cells), which are found in numerous locations throughout the body including patches/pockets within the intestinal wall, play a pivotal role at this stage. When dendritic cells encounter foreign molecules they capture them and present them to other cells (T-cells) of the immune system. In the case of an allergic individual, the immune system incorrectly identifies certain proteins as harmful. This results in the production of large quantities of allergen-specific IgE antibodies which bind to the surface of mast cells (i.e. tissue cells).
2. **Reaction:** Once sensitisation has occurred, subsequent exposure to that allergen can lead to an allergic reaction, i.e. in a sensitised individual the allergenic protein cross-links with the IgE antibodies on the surface of the mast cells causing release of histamine or other substances such as leukotrienes and prostaglandins. These result in allergic symptoms (e.g. itching, swelling). In many cases the reactions are immediate but they can take several hours to develop.[5]

Food intolerances, on the other hand, do not involve the immune system.[5,6] Food intolerances may be categorised as enzymatic (e.g. due to an enzyme deficiency such as lactase which is required to digest the milk sugar lactose), pharmacological (e.g. due to amines such as histamine) or in some

cases the mechanism may be undefined.[7]

This review deals only with food allergy.

2. Prevalence of allergies in Europe

The EuroPrevall study has been one of the most comprehensive research projects to evaluate the prevalence, basis and cost of food allergy. This multi-disciplinary project which was funded by the European Union was launched in 2005 and completed in 2009. It involved partners from Europe and world-wide.[8,9] Regarding prevalence, there were 2 elements to this research: i) a literature review of more than 900 published studies on the prevalence of food allergies in Europe and ii) an actual study to establish the true percentage of infants, children and adults with food allergies across Europe.

Of the 900 published studies, only 51 studies were conducted on a representative sample and could therefore be used to estimate prevalence.[10] These studies reported prevalence to allergies in any food (i.e. they were not confined to specific foods). In some studies, the food allergy was confirmed by a challenge test, a skin prick test or a blood test; however, in most studies the food allergy was self-reported. In studies where the food allergy was clinically confirmed, the percentage of people reported to have an allergy ranged from 1 to 5%. In the other studies (i.e. self-reported food allergy), the percentage ranged from 3 to 38%. However, only 1 to 11% of these people had their allergy confirmed. This shows the discrepancy between the percentage of people who think they have an allergy and the percentage of people who are actually diagnosed as allergic. Due to the high variability in results between studies and other limitations with the data, it was not possible for the researchers to use these data to calculate the overall percentage of people in the European Community with food allergies.[10]

The EuroPrevall study also established the true percentage of infants, children and adults with food allergies across Europe, through the EuroPrevall Birth Cohort and Community surveys. For the EuroPrevall Birth Cohort Study, a total of 12,049 babies and their families were recruited from 9 different countries. [(11)] Using standardised questionnaires and clinical assessments, this study investigated: i) the occurrence of food allergies in the first 2½ years of life, ii) regional patterns of food allergy and iii) the role of parental, pre-natal and early life risk and protective factors. The researchers found considerable differences between countries for a range of factors that are hypothesised to play a role in the development of food allergies. These included family history, obstetrical practices and pre- and post- natal environmental exposure.

The UK Food Standards Agency (FSA) is also involved in studies concerning food allergy and food intolerance.[12] One of the studies funded by the FSA aimed to generate robust data on the prevalence of food allergy and food intolerance, in UK children, and to compare these data with previous estimates to see if the prevalence is changing over time.[13] In this study a whole population cohort of children on the Isle of Wight was followed from birth to 3 years of age. A total of 969 pregnant women were recruited for the study (i.e. 91% of the target population). Over the course of the 3 years, 942 children (i.e. 97.2% of the target population), were seen at either 1, 2 or 3 years of age; while, 807 children (i.e. 83.3% of the target population) were seen every year. Whole population cohorts of older groups, i.e. children aged 6 years (n=1440, 100% of the target population), 11 years (n=775, 47.4% of the target population) and 15 years (n=757, 50.2% of the target population) were also recruited. Data were collected using detailed questionnaires and reported food allergies were confirmed via skin prick testing and controlled food challenges. The study found that the prevalence had not changed over the past two decades. Furthermore, the study found that reported food allergies were common in all age groups; however, the percentage of confirmed food allergy was much lower (based on double blind placebo controlled food challenge and a good clinical history, it

ranged from 3% for one year olds to 1.4% for eleven year olds). Based on this discrepancy the need for accurate diagnosis to prevent children being placed on unnecessary restricted diets was highlighted. Other published reports from the Isle of Wight indicate that the prevalence of food allergies shows a significant drop between the ages of 4 and 10 years (5% prevalence at 4 years compared to 2.3% at 10 years) followed by a significant rise between 10 and 18 years (4% at 18 years).[14]

Other studies have shown that around 5 – 8% of children and 1 – 2% of adults are affected by food allergy.[15,16] The prevalence of food allergy in the United States was reported to be 8% for children (i.e. those less than 18 years of age).[17]

3. Foods implicated in allergic responses

More than 120 foods have been described as causing food allergies, but only a limited number of those cause most allergic reactions.[10,18] The most common causes of food allergy in the UK and the US are peanuts, tree nuts, eggs, fish, cows' milk, crustacean/molluscs/shellfish, soya beans, and cereals containing gluten[16], although this pattern varies across Europe and internationally.[19] The EuroPrevall study found that fruits (e.g. peach) and nuts (e.g. hazelnut) were the most common allergen sources, often in association with pollen.

Although many foods or groups of foods can trigger an allergic reaction, 14 substances or products require mandatory allergen labelling under EU law (i.e. Regulation No 1169/2011). Two of these ingredients (gluten containing cereals and sulphur dioxide/sulphites) do not result in IgE-mediated immune reactions but are termed allergens to simplify the legislation. These 14 specific ingredients (including those carried over in processing aids, additives and solvents) represent those that were the most common or serious causes of food hyper-sensitivity in the EU at the time the legislation was developed and must be declared on the label when they are used in the production of a foodstuff. Declaration is not specifically required where one of the 14 ingredients is found at low levels as a result of cross-contamination in a food, though the management of this situation is not harmonised throughout EU Member States and therefore handled in accordance with risk assessments in each individual jurisdiction.

Further detail on allergen labelling is provided in section 7.2.

4. Symptoms of food allergies

Symptoms range from mild to severe. Different organs such as the skin, gastrointestinal tract, respiratory tract, eyes and central nervous system can be affected. Itching and/or swelling of the mouth are the most common symptoms. Anaphylaxis which causes severe and life-threatening reactions occur in a small number of cases. Fortunately, most allergic reactions to food are relatively mild.[6,21]

Anaphylaxis is an acute, potentially life-threatening condition. It can involve the cardiovascular system, the respiratory tract, the mouth, the pharynx and the skin, either singly or in combination. The initial symptoms often involve the skin or the oropharynx (i.e. the mouth region). Skin symptoms include development of a rash/hives, angioedema (i.e. swelling beneath the skin) and pruritus (i.e. itchy skin). Symptoms from the mouth region include tingling and pruritus of the lips. Oedema (i.e. swelling) of the larynx can cause difficulties swallowing and talking. Respiratory function may also be severely compromised. Respiratory symptoms include bronchospasm, cough and wheezing. These symptoms are often mistaken as worsening of pre-existing asthma. In some cases, the initial symptom may be loss of consciousness.[22]

“Anaphylactic shock” is a serious condition in which blood pressure drops rapidly and the sufferer could die from cardiac arrest unless adrenaline is administered soon after symptom onset in order to open up the airways and reverse vasodilation.[6] Data collected in England and Wales since 1992 suggests that 20 deaths annually are attributed to anaphylactic reactions and that about one quarter of these reactions are due to foods.[23] Anaphylactic reactions to food are associated with IgE-mediated allergy. In Europe, peanut is the most commonly implicated foodstuff[24]; however, other food allergens may also cause anaphylactic reactions.[22]

5. Diagnosing food allergies (Skin tests, Food elimination diets, RAST, DBPCFC)

As highlighted in section 2, the percentage of people who think they are allergic (i.e. are self-diagnosed) is higher than the percentage of people who are actually diagnosed. This discrepancy highlights the need for accurate diagnosis to avoid unnecessary dietary restrictions and to provide reliable prevalence data.[25]

The first step in the diagnosis of a food allergy involves a medical specialist taking a full clinical history and performing a clinical examination. Special attention is given to the type, frequency and time of occurrence of the symptoms. Specific diagnostic methods include skin prick tests, blood tests, oral food challenge tests, double-blind placebo-controlled food challenge tests (DBPCFC) and food elimination diets. Each test has its advantages and disadvantages.[5,25-27]

1. Skin prick testing and blood tests are the first tests used for the detection of food-specific IgE antibodies.[25,27] Skin prick tests are cheap and usually safe even in the case of severe nut allergy. Furthermore they can be performed at the first visit and the results are readily available. For this test a small drop of the allergen is placed on the skin, usually the forearm and the skin is pricked through the drop with a lancet. The reaction of the skin to the allergen indicates whether the patient has IgE antibodies and is thus sensitive to that allergen. However, ‘false negatives’ can occur.[25-28] Blood tests such as the radioallergosorbent test (RAST), on the other hand, measure levels of specific IgE antibodies to suspected or known allergens. The likelihood of a clinical reaction increases with increasing IgE levels.[26]
2. Oral food challenge tests require the patient to eat a suspected food in gradually increasing amounts under controlled conditions to see if allergic symptoms occur. These tests must be performed under medical supervision. For older children and adults, double-blind placebo-controlled food challenge tests (DBPCFC) are normally conducted, i.e. neither the patient, nor the investigator knows whether the challenge materials contain the specific food allergen under investigation. Although this is the gold standard in food allergy diagnosis, ‘false negative’ results can occur, particularly if the highest dose used is too low. It is therefore recommended that this test is followed by an open (i.e. unblinded) challenge test, if negative.[27]
3. The elimination test involves removal of suspected food(s) from the diet for approximately two weeks. If the symptoms disappear, suspected foods are added back to the diet, one at a time, in small but gradually increasing amounts until a normal consumption pattern is achieved. During this period symptoms are monitored. Once all the suspected foods have been checked out, foods causing problems can be avoided.[5]

6. Factors influencing the prevalence of food allergies

Although genetic factors undoubtedly contribute to the development of food allergies[29], evidence suggests that genetic factors are not solely responsible. Studies have found that populations with similar genetic backgrounds may have different prevalence of food allergies and vice versa.[30] Thus it

appears that prevalence is related to a myriad of genetic, environmental and demographic factors.[31]

This section focuses on four specific factors: i) increased exposure to new foods, ii) geographical differences, iii) developments in food processing and iv) developments in food technology.

6.1 Changes in dietary habits

In this era of globalisation, where world-wide travel is common and foods are traded globally, consumers are routinely exposed to new foods and thus dietary habits are changing.

Over the past 30 years, changes in dietary habit have been linked to an increase in peanut allergies in the western world. Qualitative findings from the EuroPrevall study back this up. Focus groups conducted in four different countries (Bulgaria, Spain, Poland, UK) revealed greater consumption of processed foods (the effect of processing on allergenicity is discussed in section 6.3), ethnic foods and an increase in snacking. Furthermore, these studies revealed a lack of consumer knowledge about the ingredients of these foods (e.g. foods that are not pre-packed and therefore do not have an ingredients label).[32] Other examples linking allergy prevalence to dietary habits include a higher incidence of sesame allergy in the Middle East and Israel and a higher incidence of rice allergy in China and Japan.[8]

6.2 Geographical differences

Geographical differences in allergen prevalence may also be attributed to factors other than dietary habits. For example, a higher incidence of apple allergies occurs in Northern Europe where birch trees are commonly found.[33] This may be explained by the similarity between the allergenic proteins found in apples and birch trees. Apples contain two major allergenic proteins and one of these Mal d 1, closely resembles the Bet v 1 allergenic protein found in birch pollen. Thus people sensitive to birch pollen may also react to apple flesh.

6.3 Food processing

Before discussing the effect of food processing on food allergens, it is important to understand the interaction between the allergenic protein and immunoglobulin E (IgE) antibodies.

As stated in section 1, an allergic response is initiated in a sensitive individual when an allergenic protein cross-links with IgE antibodies on the surface of mast cells causing release of histamine or other substances such as leukotrienes and prostaglandins.[5] The part of the protein responsible for IgE cross-linking is known as the epitope. The epitope may constitute a simple structure, i.e. a stretch of a few amino acids along the primary structure (linear epitopes) or it may be a more complex three dimensional structure (conformational epitope). More than one epitope is required for IgE cross-linking. Some allergenic proteins contain multiple copies of the same epitope; while, others may have several different epitopes.[35] Changes to the epitope (e.g. any modification, deletion or substitution of amino acids) may influence its ability to cross-link with IgE and this may influence allergenicity.[34,35] In certain circumstances, food processing can alter the epitope and thus alter the allergenicity of foods.[34-37] It can lead to epitope destruction, modification, masking or unmasking thereby decreasing, increasing or having no effect on allergenicity.[35] The effect is influenced not only by the molecular properties of the allergen but also the type of processing and the interaction between the allergen and other food components.[34]

Some thermal processes (e.g. cooking, baking, grilling, drying and sterilisation) can influence allergenicity. High temperatures can lead to epitope destruction as a result of protein denaturation; however, some allergenic proteins, such as the peanut allergen Ara h 1, may be thermostable.[38] The

type of thermal process is also significant, e.g. it has been shown that the allergenicity of peanuts (Virginian variety) is lower in boiled than roasted peanuts. This has been attributed to the loss of low molecular weight allergens into the water.[39] Furthermore, the interaction with other proteins, fats and carbohydrates in the food matrix can also influence allergenicity. One example is the Maillard reaction, which is the chemical interaction between amino acids and sugars during heating (or storage). In milk, the interaction between the protein beta-lactoglobulin and the sugar lactose increases allergenicity.[40]

Proteolysis (breakdown of proteins into smaller polypeptides or amino acids) can also influence allergenicity. Proteolysis can be achieved through the use of enzymes such as proteases and has been used to decrease the allergenicity of soybean.[41] Physical removal of the allergenic component is another means of decreasing the allergenicity of foods. For some foodstuffs a combination of techniques is used. For example treatment of milk with proteases followed by ultrafiltration is used to prepare hypoallergenic products such as infant formulae; while a combination of enzyme and heat treatment has been shown to reduce the allergenic potential of hen's egg 100 fold.[36]

These findings highlight the opportunities and challenges facing food processors in reducing and eliminating food allergens.

6.4 Biotechnology (Genetically modified foods)

The manipulation of plants, animals or microorganisms so that they possess particular characteristics is possible through the identification, isolation and manipulation of individual genes or groups of genes that are responsible for specific physical or metabolic traits (i.e. genetic modification or engineering).

From a safety perspective genetically modified (GM) food is one of the most scrutinised food types. Prior to being placed on the market, GM foods undergo a safety assessment by the European Food Safety Authority (EFSA) which includes an assessment of allergenicity of the new trait. Member States and the public can comment on both the application and the EFSA safety assessment. A Standing Committee of experts from Member States decides on whether to authorise a GM food or not. GM food authorisation is for a period of 10 years; however, the authorisation must be renewed if the food is to remain on the market any longer. This process ensures that GM foods allowed on the EU market are as safe as their non-GM counterparts. This process is outlined in the GM Food and Feed Regulation (EC No. 1829/2003).[42]

GM technology can also be used to remove allergens from foods, e.g. the production of soy products that would pose a smaller risk of food allergies than standard soybeans.[43]

7. Management of allergen risks by the food industry

The food industry has a legal obligation to produce safe food for consumers (Article 14, Regulation No. 178/2002). Regarding allergens, the food industry achieves this through:

i) The implementation of a food safety management system based on principles of Hazard Analysis and Critical Control Point (HACCP).
ii) Labelling of foodstuffs to inform the consumer of the presence of allergens.

Many challenges are faced by the food industry in the management of allergen risk; e.g. lack of threshold values and quantitative legislative guidance and also, lack of validated analytical methods for allergen detection. These issues are discussed below.

7.1 HACCP

HACCP is a food safety management system which ensures potential hazards (i.e. biological, physical and chemical hazards) are identified and strategies are put in place to control them before they threaten the safety of the food. HACCP forms the foundation of European (Articles 4 & 5 of Regulation 852/2004)[44] and international food legislation and is a key component of global trade in food products. Today, food industry standards play a major role in assisting food businesses to achieve compliance with legislation and in many cases exceed legislative requirements. Furthermore, they enable food businesses to ensure consistency in terms of product safety and quality.

Allergen management is an integral part of a food business' food safety management system to manage potential risks from food allergens. Allergen management covers all aspects of the business from sourcing and handling of the raw materials through manufacturing, processing and packaging of the finished product. It is also an important consideration during new product development.[45]

One of the biggest challenges for the food industry is the avoidance of cross contamination between ingredients/foods known to be allergenic and non-allergenic ingredients/foods. For example, in many manufacturing premises production lines dedicated to the manufacture of a single product are not always feasible or practical for commercial or other reasons.[46] Therefore, cleaning of shared equipment, processing lines and the local environment is one of the critical points for effective allergen control. Manufacturers define cleaning procedures and cleaning schedules appropriate for their facilities (e.g. wet/dry cleaning) and these are then validated (to ensure the cleaning programme is effective) and verified (to demonstrate that the validated cleaning procedures have been properly performed).[47]

7.2 Labelling

Legislative requirements
Labelling is essential to assist consumers, who have allergies or intolerances, by providing them with information on the composition of foodstuffs. Although many foods or groups of foods can trigger an allergic reaction, only 14 substances or products require specific allergen labelling under EU law (i.e. Regulation No 1169/2011). These allergenic ingredients (including those carried over in processing aids, additives and solvents) must be indicated on the label of a foodstuff:

1. Cereals containing gluten and products thereof
2. Crustaceans and products thereof
3. Eggs and products thereof
4. Fish and products thereof
5. Peanuts and products thereof
6. Soybeans and products thereof
7. Milk and products thereof (including lactose)
8. Nuts i.e. almond, hazelnut, walnut, cashew, pecan nut, brazil nut, pistachio nut, Macadamia nut and Queensland nut and products thereof
9. Celery and products thereof
10. Mustard and products thereof
11. Sesame seeds and products thereof
12. Sulphur dioxide and sulphites at concentrations of more than 10mg/kg or 10 mg/litre expressed as SO2
13. Lupin and products thereof
14. Molluscs and products thereof

The scientific justification for mandatory labelling of these allergenic ingredients has been provided by the EFSA Scientific Panel on Dietetic Products, Nutrition and Allergies (NDA). However, it is important to note that specified derivatives of some of these 14 substances and products may be exempted from this labelling requirement, if based on an opinion by EFSA it has been concluded that they are not likely to result in an adverse reaction in susceptible individuals. The current exemptions are listed in European legislation, i.e. Regulation (EU) No 1169/2011. This list is reviewed on an on-going basis in light of changing dietary habits, food processing practices as well as the emergence of new scientific and clinical findings. EFSA is currently mandated through a request from Ireland to review all of the allergens on this list with respect to their prevalence, threshold concentrations and analytical methods for their detection/quantification (EFSA Register of Questions: Mandate M-2011-0194, Question Number EFSA-Q-2011-00760).

From 13th December 2014, new rules[20] regarding allergen labelling are in force. Firstly, the name of the allergen must be clearly distinguished from the other ingredients on the label of pre-packaged foodstuffs, e.g. by font, style or colour. Secondly, allergen information must be provided for non-prepacked food (i.e. foods sold loose in restaurants, take-away foods, deli counters, food stalls etc). This new requirement is particularly important considering that most food allergy incidents are linked to non-prepacked food and food eaten outside of the home. The legislation is not prescriptive in terms of how this information should be provided for non-prepacked foods, it simply states that the exact requirements should be established in national law.

Voluntary precautionary labels

Although every effort is taken by industry to eliminate the risk posed by the unintended presence of food allergens, in many businesses it is virtually impossible to produce a zero risk product. Thus precautionary labelling such as ‘may contain…..’or ‘prepared in a factory that uses……’ are sometimes used by manufacturers if they consider that unintended allergens may be present in amounts that could pose a risk. However, it is important to note that precautionary labelling cannot replace the allergen management system that each food business is obliged to have in place as part of its food safety management system. Hence labeling of unintended allergens should only take place in situations where the risk of unintended presence is real and cannot realistically be expected to be kept under control. Furthermore, although no specific legislation currently exists on precautionary labelling, legislation is expected in the future once the relevant EFSA mandate has been completed, i.e. the European Commission is expected to adopt an implementing act dealing with this matter.[20] Currently, there are two main issues surrounding voluntary precautionary labelling:

1. The absence of allergen safety thresholds (i.e. the minimum dose that can elicit a reaction in a substantial proportion of vulnerable consumers) and labelling thresholds (i.e. the level above which requires a specific declaration on the product packaging) has been problematic for manufacturers and has resulted in inconsistencies in the application of precautionary labelling. It has also been problematic for regulators, with the result that the attitude and reaction to the unintended presence of low levels of undeclared allergens in foods varies considerably within the EU.
2. When applied prudently, precautionary labels can help protect vulnerable consumers. However the unwarranted use of precautionary labels can: i) result in the unnecessary elimination of healthy options from the diet of allergic consumers or ii) reduce their credibility causing vulnerable consumers to take risks with these foods. Regarding the latter, a study of British parents of children with nut allergy found that many either ignored warning labels on foods or assumed that the wording (e.g. 'not suitable for nut allergy sufferers 'versus 'may contain traces of nuts' etc) reflects a gradation of risk.[48]

7.3 Establishing thresholds

Allergen safety thresholds may be defined at two levels: individual thresholds and population thresholds. An individual threshold is the maximum amount of an allergen that can be tolerated by an allergic individual. A population threshold, on the other hand, is the maximum amount of an allergen that can be tolerated by the entire population (or a representative sub-population) of individuals with that food allergy. However, the establishment of population thresholds which protect all sensitive individuals is virtually impossible and thus the establishment of population thresholds, which avoid serious reactions in the vast majority of sensitive individuals are more realistic. Population thresholds can help both the food industry and regulatory authorities assess the public health risk and design appropriate food safety objectives to guide risk management.[49] For example, they could provide a scientific basis for effective and consistent mandatory and precautionary labelling.

In recent years, progress has been made in filling the data gaps, which prevented quantitative risk assessments and thus the establishment of safety thresholds. Tools to analyse these data have also been developed (nowadays statistical modelling of dose distributions is a commonly accepted approach for characterising hazards arising from allergens, so also are probabilistic approaches for estimating the likely consequences of a particular pattern of allergen contamination). Other progress includes a practical approach to allergen risk assessment, known as VITAL (Voluntary Incidental Trace Allergen Labelling), which was initially developed by the Australian Allergen Bureau in 2007 (VITAL 1.0) and was updated in 2012 (VITAL 2.0). VITAL is a risk based methodology for assessing the impact of allergen cross contact and providing appropriate precautionary allergen labelling. It uses an action grid which assists in determining if the presence of residual allergenic proteins through unavoidable cross contact requires a precautionary labelling statement.

Considering these developments and being mindful of the remaining data gaps, the Food Allergy Task Force of International Life Sciences Institute (ILSI) Europe has formed an expert group with the aim of developing a consensus on quantitative action levels for use in the management of allergenic foods. In September 2012, ILSI Europe hosted a workshop ’From Threshold to Action Levels’ inviting leading experts to reach a consensus over the feasibility of defining threshold levels, the approaches to be used and the data and knowledge gaps are still to be addressed.

7.4 Analytical methods for allergen detection

Reliable methods to detect and quantify allergens are required by the food industry to validate cleaning procedures[50], to ensure compliance with food labelling and to improve consumer protection.[51,52] They are also important for regulatory authorities to assess compliance of foodstuffs with legislation (i.e. general food safety legislation and labelling legislation).[50] Five criteria, i.e. accuracy, precision, sensitivity, specificity and reproducibility, are commonly used to determine reliability.[52] ELISA (enzyme-linked immunosorbent assay) and DNA-based polymerase chain reaction (PCR) are the main methods used for the detection and quantification of food allergens.[53]

The ELISA method is based on antigen-antibody interactions to allergenic proteins. This method is specific, sensitive, has low limits of detection/quantification and is rapid. However, it is very matrix specific and because it relies on protein-antibody interaction it is susceptible to producing false negative results. Other antibody-based technologies (e.g. dipsticks and lateral flow devices) are also useful for rapid analysis, particularly when testing is required outside of the laboratory (e.g. for monitoring the effectiveness of cleaning procedures).[50]

DNA-based polymerase chain reaction (PCR) is a method used to detect and quantify DNA. This

method is useful for allergen detection/quantification in processed foods as DNA is generally more robust than protein and is therefore less likely to be damaged or destroyed during processing. Using this technique the selected DNA is amplified, making it particularly appropriate for use when very small quantities of the food allergen source are present. Furthermore, the correct selection of primers (portions of nucleic acid that serve as a starting point for DNA synthesis) ensures this technique is highly selective with a lower chance of false positives.

Method validation is an integral part of any good analytical practice and is essential to ensure the method is fit for purpose. The European Commission's Joint Research Centre (JRC) has co-authored new international guidelines on Validation Procedures for Quantitative Food Allergen ELISA Methods. The aim of this guidance is to promote harmonised, accurate and reliable testing of potentially lethal food allergens by analytical laboratories worldwide.[54] To date, ELISA test kits have been validated for defined matrices, i.e. specific allergens in specific foodstuffs (e.g. peanut in cereals, cookies, ice cream and chocolate).[50] DNA based methods have also been validated for certain allergenic materials, particularly where ELISA technology has proved difficult to develop, such as for celery where cross-reactivity with many other edible plants of the same family occurs (Method CEN/TS 15634-2:2012).

8. Allergy prevention strategies – the dietary approach

The only way to prevent an allergic reaction is to avoid foods that cause signs and symptoms; however, research is focusing on the prevention of initial sensitisation. Despite much research and many intervention studies, no approaches currently achieve this aim.

Evidence suggests that development of tolerance to allergens requires early colonization of the intestinal tract by appropriate microflora.[55,56] This has led to investigations using, for example, probiotics (live microorganisms which may provide a health benefit in humans when consumed) and/or prebiotics (food components that may provide a health benefit when consumed because of changes they may bring about to the gut bacterial flora). Although evidence exists that Lactobacillus rhamnosus may reduce the incidence of eczema in infants, evidence linking other probiotics to the prevention of other allergies is lacking. Furthermore, there are questions about whether the effects are transient or long-lasting. The situation is similar for prebiotics. Considerably more research is needed in this area before conclusions can be made.

Numerous studies have investigated the beneficial effects of breastfeeding on allergy prevention. The European Academy of Allergy and Clinical Immunology (EAACI) recommends exclusive breastfeeding for the first 4-6 months of life to prevent the development of allergic diseases including food allergy. In the absence of breast milk, formula with hydrolysed proteins and documented reduced allergenicity should be used for at least 4-6 months for infants at increased risk of allergic disease (i.e. infants whose mother, father or sibling(s) have an allergy).[57,58] Different meta-analyses suggest a strong link between breastfeeding for at least 3 months and reduction in the risk of atopic dermatitis; however, the evidence is weaker for food allergies and thus further research is required.[59-61] Despite this, the importance of breastfeeding as a source of nourishment for infants cannot be underestimated.

Conflicting evidence exists regarding the relationship between maternal consumption of allergens (e.g peanuts) during pregnancy and subsequent food allergy in the baby. One hypothesis currently being investigated is the possibility that some food allergies arise through cutaneous or respiratory exposure and that oral exposure through eating is actually protective, leading to the development of tolerance. This hypothesis underlies the LEAP study (Learning Early about Peanut allergy) and the EAT study (Early Acquisition of Tolerance).[62-63]

Other dietary factors epidemiologically linked with allergic disease include polyunsaturated fatty acids and antioxidants such as vitamins (C, D & E), zinc and selenium.[64] For example, Vitamin D deficiency has been linked to food induced anaphylaxis; e.g. birth during winter months has been associated with a modest increase in food induced anaphylaxis.

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