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Nutritional Issues in Food Allergy

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Abstract

Diet and nutrition play an important role in the development and management of food allergy. The diet of expectant mothers can have an effect on their offspring in terms of allergic outcomes. A host of confounding factors may influence this, with a maternal diet rich in fruits and vegetables, fish, vitamin D-rich foods associated with a lower risk of allergic disease in their children. More surprisingly, the consumption of milk and butter has also been shown to have a protective effect, especially in a farm environment. Similarly, the diet of the infant can also be important, not only in terms of breast feeding, but also the timing of the introduction of complementary foods, the diversity of the diet and the effect of individual foods on the development of allergy. One factor which has clearly been shown not to influence the development of food allergy is allergen avoidance by expectant mothers. In the infant diet, the manipulation of the gut microbiome to prevent the development of atopic disease is clearly an area which promises much, although studies have yet to provide a breakthrough in the prevention of atopic dermatitis. More concrete evidence of the value of diet in prevention has come from studies evaluating infant eating patterns which may protect gut health, through the consumption of large amounts of home-processed fruits and vegetables. The consumption of fish during the first year of life has also been shown to be protective. The importance of nutritional issues in children and adults who have a food allergy has become much more accepted in recent years. The primary allergenic foods in infancy and childhood, milk, egg, wheat and soy are also ones which are present in many foods and thus their avoidance can be problematic from a nutritional perspective. Thus, children with a food allergy can have their growth compromised through avoidance, especially pre-diagnosis, when foods may be excluded without any expert nutritional input. The management of a food allergy largely remains the exclusion of the offending food(s), but it is now clear that in doing so, children in particular can be at nutritional risk if insufficient attention is paid to the rest of the diet. Adults with food allergy are often thought not to need nutritional counselling; however, many will exclude a wide range of foods due to anxiety about trace exposure, or similar foods causing reactions. The avoidance of staple foods such as milk and wheat are common, but substitute foods very often do not have comparable nutritional profiles. Adults may also be more susceptible to on-line promotion of extreme nutritional regimes which can be extremely harmful. All food allergic individuals, whatever their age, should have a nutrition review to ensure they are consuming a healthy, balanced diet, and are not avoiding food groups unnecessarily.

Keywords Nutrition · Allergy · Diet · Food · Prevention

Introduction

The concept of nutrition being an important medicinal tool is nothing new. Hippocrates said "Let food be thy medicine and medicine be thy food." In the twenty-first century, in an age of global information accessibility, there are many different opinions regarding the efficacy of food and nutrition in treating medical problems, or simply providing important health benefits. However, these can be hard to interpret, and parents and patients will often turn to frontline staff working in food allergy to get an authoritative opinion. For example, prospective parents will often wish to know what foods or supplements taken during pregnancy can best prevent the allergy in their children. They will also ask about the infant's diet, which milk should be offered if breast milk is not an option and the timing of the introduction of complementary foods. However, food is probably the more important medicine when it comes to the management of food allergy. Dietary elimination has long

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been the only way to manage food allergic individuals, and although the last 15–20 years has seen a rise in immune-modulatory treatments for food allergy, most patients still have to exclude one or more foods to the detriment of their nutritional status. This paper will examine the evidence for the role of the maternal diet in the development of allergic outcomes in their offspring, and also whether diet in infancy can influence the allergic trajectory. The paper will then discuss the issue of nutrition and growth in allergic children, and the consequences of exclusion diets in children and adults, providing evidence that the dietary management of food allergy may have unwelcome consequences.

Nutritional Issues in the Development and/or Prevention of Food Allergy

The Maternal Diet

The effect of the maternal diet may be to promote tolerance to key dietary antigens in the unborn child. A review by Jeurink and colleagues concluded that the presence of maternal dietary proteins in amniotic fluid, cord blood and human milk might support the induction of tolerance to solid foods in infants [1]. Many studies have examined the effect of the maternal diet on the development of food allergy in infants, but currently, it is not clear whether any one nutrient is more important in terms of preventing food allergy. One recent study reported that the inclusion of foods containing vitamin D in maternal diets during pregnancy may reduce the likelihood of allergic rhinitis in the offspring [2]. Studies have also evaluated whether supplementation can have adverse effects. Parr and colleagues reported that children born to mothers with the highest total folate intake from diet and supplements had a 23% greater risk of asthma at age 7 years than those born to mothers with the lowest total folate intake [3]. McStay and colleagues reviewed the evidence for the effect of folic acid supplementation and the promotion of an allergic phenotype in the offspring, concluding that results from different studies are conflicting and inconclusive, and randomised controlled trials (RCT) are needed to establish optimal timing of supplementation [4]. The key to understanding whether individual nutrients are protective or adversely affect the outcome of pregnancy may be not the level of supplementation but how the nutrients are delivered. Tukkola et al. reported an increased risk of developing cow's milk allergy (CMA) in the offspring of women taking vitamin D and folate supplements, whereas vitamin D intake from foods during pregnancy was associated with a decreased risk of CMA [5].

In addition to vitamins, the quality and quantity of fats and fatty acids in the maternal diet may be important. Large national datasets suggest that women who are pregnant or of childbearing age may have low intakes of omega 3 long chain polyunsaturated fatty acids (n-3 LCPUFA), especially those from socioeconomically disadvantaged populations [6]. However, a Cochrane review and meta-analysis in 2015 concluded the evidence to support supplementation of pregnant women with n-3 LCPUFA was limited, with few differences in childhood allergic disease between women who were supplemented and those who were not [7]. More recently, a meta-analysis by Best and colleagues found that increased n-3 LC-PUFAs in the maternal diet did result in beneficial outcomes in terms of childhood allergic disease, but the results were inconsistent [8]. For example, one large review of children at the age of 6 years found no difference in allergy outcomes between children whose mothers were supplemented with n-3 LCPUFA and those who were not [9]. In contrast, another study involving 695 children whose mothers had received 2.4 g of n-3 LCPUFA (fish oil) or placebo (olive oil) per day in the third trimester of pregnancy found that the risk of persistent wheeze or asthma in the treatment group was 16.9 versus 23.7% in the control group, corresponding to a relative reduction of 30.7% [10].

A systematic review by Saadeh and colleagues reiterated the importance of evaluating the whole diet and nutritional patterns, so that the complex interactions of nutrients eaten together could be assessed [11]. A more recent review examined the role of nutrition in the first 1000 days after conception, concluding that an unhealthy diet during pregnancy, mainly characterised by a high-fat intake, can result in alteration of foetal lung development and carry an increased risk of respiratory disorders [12]. In contrast, the Mediterranean diet was associated with a lower risk of allergic sensitisation and allergic rhinitis. However, Castro-Rodriguez and Garcia-Marcos reported that although adherence to the Mediterranean diet during pregnancy did show some protective effects on asthma/wheeze in the offspring, this only lasted during the first year of life, with few studies demonstrating a protective effect on wheezing, current sneeze and atopy, and none on eczema [13]. The great difficulty with studies of the maternal diet is that they are often carried out retrospectively through analysis of dietary patterns reported in food diaries. It is therefore timely that a large RCT prospectively assessing the effect of the Mediterranean diet in pregnancy on the development of allergic disease is planned, with pilot data demonstrating the feasibility of the study design and sustainability of the proposed dietary intervention [14]. The Mediterranean diet may not be the only dietary pattern of importance in prevention. Loo et al. reported that a Seafood and Noodle dietary pattern was associated with a reduced risk of developing allergen sensitization at 18 months and 3 years, whereas a vegetable, fruit and white rice pattern and pasta, cheese and processed meat pattern were not linked to any such reduction of allergic outcomes [15]. The authors suggest that the increased intake of fatty acids from the seafood and noodle diet that might be partly responsible for this outcome. However, the maternal diet may not affect allergic outcomes in every population; a study conducted in the Netherlands showed no associations between diet quality during pregnancy and food allergic sensitisation in children at the age of 10 years [16].

Another systematic review found few significant associations between maternal diet and allergic outcomes, but did report that a maternal diet rich in fruits and vegetables, fish, vitamin D-rich foods were associated with a lower risk of allergic disease in offspring [17]. Foods associated with higher risk included vegetable oils and margarine, nuts and fast food so perhaps individual foods in the diet might be more important. Results from food frequency questionnaires (FFQ) completed by the mothers in a population-based birth cohort found that overall, the consumption of milk products was associated with a lower risk of CMA, with cord blood indicating the activation of antigen-specific immunity in the infant during pregnancy [18]. The findings were especially pronounced in non-allergic mothers, with an inverse association between the high use of milk products and CMA in their offspring (OR 0.30, 95% CI 0.13–0.69, $P < 0.001$). This association with milk was also shown in another study. Mothers living on small dairy farms and those from rural but non-farming communities completed FFQ during pregnancy and 24-h food diaries during lactation. Farming mothers ate more whole (full fat) milk, butter, saturated fat and total fat than non-farming mothers, who consumed more margarine, oils and low-fat milk and whose offspring were eight times more likely to have a doctor-diagnosed allergy [19]. Other foods show a mixed response. Increased maternal egg ingestion was linked to more ovalbumin in breast milk and markers of immune tolerance in infants [20]. However, an interventional RCT did not find any effect on allergic outcomes in children of increased maternal fish intake, and this finding was supported by a subsequent systematic review and meta-analysis [21, 22].

Tree nuts and peanuts are the foods most expectant mother are concerned about; to eat or to avoid? Willers et al. reported that daily consumption of nut products increased the risk of childhood wheeze, dyspnoea and asthma symptoms [23]. However, more recent data from Järvinen and colleagues showed that maternal peanut exposure during pregnancy and lactation had no impact on peanut allergy in the offspring, when compared to no maternal exposure [24]. Maternal intake of fruits and vegetables may also be relevant; a study on 550 infants reported that higher prenatal intakes of total fruit and vegetables were associated with the decreased risk of respiratory tract infections in offspring [25]. Fruits and vegetables may have an effect due to their antioxidant properties or the fact that they could promote beneficial changes in the intestinal microbiota. Their consumption as part of a healthy or Mediterranean diet could be why such diets are beneficial.

An increasingly important influence on allergy outcomes in both mothers and their babies is the gut microbiome. The mechanisms by which the maternal microbiome influences the developing foetal immune system could include alignment between the maternal and infant regulatory immune status and trans-placental passage of microbial metabolites and IgG, with short-chain fatty acids possibly influencing foetal immune development [26]. Prebiotics have been defined as "a substrate that is selectively utilized by host microorganisms conferring a health benefit", whereas probiotics are living microorganisms that have been proposed as immune-modulators of the allergic response [27, 28]. The dietary modulation of nutritional factors through pre-, pro- and synbiotic preparations will provide some exciting and novel research opportunities, but the potential beneficial effects need to be elicited through high-quality RCTs and detailed mechanistic studies [29, 30]. Kramer and Kakurma, who have published numerous reviews on maternal and infant nutrition and atopic outcomes, consider that in high-risk individuals, antigen avoidance during pregnancy is unlikely to reduce the risk of atopic diseases in the offspring [31]. Venter et al. recommend encouraging expectant mothers to eat a good amount of fish, fruits and vegetables during pregnancy and suggest that food allergen avoidance or exposure in utero or via breast milk is not a significant factor [32].

The Infant Diet

The microbiome can also influence the development of food allergy in infants, with changes to key bacterial phylotypes in infancy being associated with the development of food allergy, and clear distinctions between the microbiota of infants with IgE-mediated food allergy from those with non-IgE-mediated conditions [33]. However, a study on 527 neonates, 47% of whom were treated with probiotics, found no difference in the subsequent prevalence of atopic dermatitis [34]. Aside from the microbiome, food diversity appears to be important in the diet of infants. Less food diversity during the first year of life is associated with an increase in the risk of asthma and allergies in childhood, and increased diversity of foods in the first year of life reduces the risk of atopic dermatitis and protects against asthma, food allergy and food sensitization [35, 36]. Grimshaw and colleagues followed a cohort of 1142 infants for 2 years and reported that predictors for the development of both IgE and non-IgE mediated food allergy included mean healthy dietary pattern score [37]. The authors consider the reason for this may be the healthy eating pattern protecting gut health due to the large amounts of home-processed fruits and vegetables, the oligosaccharides therein acting as naturally occurring prebiotics and promoting gut colonisation. However, it is possible that this effect is transitory; the Netherlands group who evaluated the maternal dietary quality also assessed diet quality in infancy and reported that it had no effect on inhalant or food allergic sensitisation, or associations with eczema or asthma in children at the age of 10 years [13].

The individual components of the infant's diet may also be protective. Castro-Rodriguez and colleagues reported that children who rarely ate fruit had a higher risk of current wheezing and greater prevalence of dermatitis [38]. A questionnaire survey of 520 children reported that at the age of 10 years, the prevalence of asthma, rhinitis and any allergic symptom was lower in those children with increased intakes of fruit; twice as many children with the lowest rate of fruit intake experienced the onset of any allergic symptom, compared to those with the highest fruit intake [39]. A systematic review and meta-analysis by Hosseini and colleagues found that out of 58 studies reviewed, one half reported a protective effect of a high fruit and vegetable diet on asthma and/or wheeze, but one third reported mixed results, and eight studies failed to show any benefit [40]. The problem with fruits and vegetables is their great diversity in composition and nutritional contribution to the diet; they might be used as a marker of a healthy diet but other types of foods and nutrients may be more important.

Studies have failed to show conclusively that maternal fish oil supplementation confers benefits on the offspring; however, fish intake in children may be more protective. Pooled analysis of RCT by Zhang and colleagues suggests that consumption of fish during the first year of life reduces the risk of eczema and allergic rhinitis [20]. An observational study of 1304 Icelandic children found that the incidence of diagnosed food sensitisation was significantly lower in children who received regular fish oil supplementation [41]. Farm children were found to have significantly lower levels of food allergy than children living in the same rural area but not on a farm; the non-farm children had intakes of vitamin D, iodine and selenium which were considerably lower than current recommendations, most likely due to them eating significantly less oily fish [42].

Much focus in the last 3 years has been on the timing of the introduction of complementary foods into the infant's diet. Whilst this is not a nutritional issue, given what we know about the diversity of the diet being important, it would seem that earlier introduction of foods will inevitably lead to more complex and diverse foods and nutrients being present in the diet. Studies have shown the benefits of early introduction of peanut on allergy prevention, but the studies on introduction of egg between 4 and 6 months have shown mixed results [43–46]. Jonsson and colleagues reported that, in their cohort of farm children, a lower risk of allergy development was associated with early exclusive breastfeeding, whereas late introduction of fish and eggs carried a greater risk of allergic outcomes [47]. However, results from the GUSTO cohort found that food allergy rates in Singapore are low despite delayed introduction of allergenic foods [48]. These conflicting results demonstrate that in food allergy, one size does not fit all, with geography, infant feeding practices and other factors impacting on the likelihood of early or late introduction of complementary foods affecting the onset of food allergy. The current advice for complementary feeding is variable, but the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) Committee on Nutrition recommend that allergenic foods may be introduced any time after 4 months, with infants at high risk of peanut allergy having peanut introduced between 4 and 11 months [49].

Nutritional Issues in Food Allergy

Nutritional Issues in Children with Food Allergy

Nutrition may play a role in the prevention of food allergy, but it is vital to consider its adequacy when implementing exclusion diets for the diagnosis and/or management of food allergy. Published research on dietary eliminations is limited by the difficultly in performing RCTs in subjects for ethical reasons [50]. Strict avoidance of certain food groups can equate to avoidance of key nutrients, and it is essential that these nutrients are obtained elsewhere in the diet in order for good health to be maintained. A small number of foods account for the majority of food allergic reactions in young children: cow's milk and egg are usually the predominant cause of IgE-mediated food allergy in the first 10 years of life, with peanut and tree nuts becoming more prevalent after this, and wheat and soy involved in both IgE and non-IgE mediated food allergy [51, 52]. Thus, nutritional adequacy can be problematic since these foods either provide a major portion of the nutrients in the diet or are present in many foods and their avoidance thus depletes the diet of variety, severely limits dietary choices and can have long-term effects on eating behaviour and taste preferences see Table 1 [53, 54].

Nutritional intake can also be compromised by unsupervised dietary manipulation, restrictions due to cultural, religious or ethical observance (e.g. vegan diet), an aversion to many foods (the "fussy eater"), fear of introducing complementary foods and doubts over which foods to introduce [55, 56]. Unsupervised milk avoidance has been linked to poor calcium intake and poor bone health, with loss of bone mineral density [57]. Vitamin D deficiency rickets, in developed countries where food availability is not an issue, has been documented in children with cow's milk allergy and no dietetic input for appropriate substitutes [58, 59]. One study found 75% of children with atopic dermatitis had tried food elimination, with cow's milk and egg being the most frequent allergens excluded from the diet, despite a lack of evidence of the efficacy of dietary exclusion [60, 61]. Children with food allergy at the greatest risk of nutritional compromise are those who are already on a restricted diet such as a vegan or macrobiotic diet. A high prevalence of rickets and growth failure has been reported in infants who consume unconventional diets which may exclude vitamin D-fortified milk [55].

Table 1 Suggested replacements for excluded foods

Food excluded	Nutrients provided	Substitute foods/other sources of similar nutrients
Cow's milk	Energy, protein, calcium, B vitamins, iodine In the USA, milk is commonly fortified with vitamins A and D	Infants-extensively hydrolysed formula/amino acid formula Children over the age of 2 years and adults–plant based milk substitutes with added calcium, e.g. oat milk, almond milk, coconut milk, rice milk *N.B. Rice milk naturally contains inorganic arsenic and in the UK is not recommended for children under the age of 5 years* Goat or sheep milk products, or mozzarella cheese made from buffalo milk, are not suitable for those with a milk allergy or lactose intolerance. Wheat products are a source of energy, protein, B vitamins and calcium. Other plant foods such as legumes, broccoli and dark leafy vegetables provide B vitamins and calcium. Fish containing bones and tofu set with calcium compounds are also sources of calcium. For some individuals, especially those excluding other foods in addition to milk, supplements may be necessary to meet requirements for energy, protein and calcium.
Eggs	Energy, protein, B vitamins (thiamine, riboflavin, niacin, B6, biotin), selenium, vitamin D	These nutrients are widely found in other animal products such as meat, seafood and vitamin-D fortified milk. Egg replacement products can be purchased for use in cooking and baking. These products provide a similar consistency if a recipe calls for eggs, but do not necessarily provide much nutrition; products made from algae, yeast, pea or soy will have more nutrition than those derived from potato starch.
Peanuts and tree nuts	Energy, protein, healthy fats, a range of vitamins and minerals depending on the nut but including—B vitamins (folic acid, thiamine, vitamin B6) Vitamin E, calcium, selenium, magnesium	Other nuts that do not cause symptoms may be eaten (professional advice should be sought to determine which nuts are safe). Individuals with pollen food syndrome (PFS) can often tolerate problematic nuts when roasted. Seeds eaten in quantity will provide a similar nutrient profile to that of nuts, and healthy fats can be obtained through avocados and vegetable oils, with the notable exception being palm oil. Plant foods will provide a healthy range of vitamins and minerals.
Fruits and vegetables	Fibre, antioxidants and a variety of vitamins and minerals depending on the fruit or vegetable including—B vitamins ((folic acid, thiamine, riboflavin), vitamin C, β carotene, calcium, iron and magnesium	Only exclude those foods that cause symptoms, ensuring that a variety of other plant foods are consumed (professional advice is required to expand the diets of individuals who have self-imposed restrictions on plant food intake). Individuals with pollen food syndrome (PFS) can usually tolerate problematic foods when they are cooked, tinned or processed.
Seafood	Protein, calcium (fish bones), vitamins A and D, vitamin B12, omega 3 fatty acids, iodine	Individuals with seafood allergy are rarely allergic to all seafood. People with fish allergy may be able to eat shellfish and equally those allergic to shellfish may tolerate finned fish. Even those with shellfish allergy may be tolerant of other types of shellfish (e.g. an individual allergic to prawns (crustaceans) may be able to eat molluscs (e.g. clams, mussels, scallops or oysters). Professional advice is required to determine which foods are safe. Flaxseeds / linseeds are a source of omega 3 fatty acids, as are animal products to a limited extent. Iodine is added to iodized table salt. Seaweed, milk and eggs are other sources of iodine.
Soy and other legumes	Energy, protein, fibre, B vitamins, calcium, magnesium, iron and zinc	Soy and other legumes, along with nuts, are a significant source of protein in plant-based diets. Whole grains are also an important source, particularly when eaten in conjunction with legumes. It is therefore important that only those foods causing symptoms are avoided (professional advice should be sought to determine which foods are safe).
Wheat and other grains—especially whole grains	Energy, protein, fibre, B vitamins (folic acid, niacin, pantothenic acid, riboflavin, thiamine, B6), iron, magnesium, phosphorus, selenium, zinc	There are a variety of grains available for cooking and baking, and many products are now made wheat-free, though professional advice should be sought to determine safe, nutritious alternatives. Milk and eggs provide energy, protein, calcium and B vitamins. Fibre can be obtained by consuming other whole grains and plant foods. The best source of iron is meat; it is in some plant foods to a lesser extent, though iron supplementation may be required in plant-based diets to meet requirements. Those avoiding both milk and wheat, especially if vegetarian may need supplements of B vitamins, calcium, iron and trace minerals. Their diets will also be low in protein and energy.

Parental delay in introducing complementary foods may occur in children with food protein-induced enterocolitis syndrome (FPIES), due to the risk of multiple food triggers including milk, soy, rice, oats or even poultry, meats, legumes, fruits and vegetables, increasing the risk of inadequate nutrient intake, especially iron in the breastfed infant [62, 63].

Children with multiple food allergies have a higher risk of impaired growth and an increased likelihood of inadequate nutrient intakes than children without food allergies [64]. Meyer et al. showed that children with food allergies in the UK are more underweight than children in the general UK population, which appears to be linked to the number of foods excluded [65]. Studies in other countries have also found food-allergic children to be smaller than their non-allergic peers when growth charts are compared to the national average [66, 67]. Thus, faltering growth may be indicative of malnutrition in those with a food allergy, although correct use of diagnostic elimination diets might actually improve nutritional status. A prospective, observational study on 130 children required to follow a 4-week supervised elimination diet for suspected food protein induced gastrointestinal allergies, achieved a statistically significant improvement in growth parameters at the end of the elimination period which was considered to be due to dietary advice, including the use of hypoallergenic formula and vitamin and mineral supplementation, and was not affected by the type of elimination diet or number of foods eliminated [67]. The algorithm shown in Fig. 1 illustrates the red flags which if present when assessing the infant or older child warrant nutritional surveillance and intervention.

The nutritional issues with elimination diets can depend on which foods are being avoided—see Table 1. In one study, those with CMA had lower intakes of calcium, zinc and vitamin B2, whereas those avoiding wheat and soy had reduced calcium, phosphorus, iron, potassium, zinc and B vitamins (vitamin B2, vitamin B6 and niacin) in their diet [68]. Cow's milk contributes significant macro- and micronutrients that are essential for normal growth and development, especially during early childhood [69]. These include energy, protein, B vitamins and especially calcium, an important micronutrient for the development of bones and teeth. Studies have shown that milk products have a favourable effect on bone health in childhood and adolescence; thus, the exclusion of cow's milk may pose problems for infant nutrition [70]. Berry et al. reported that mean anthropometric measurements in 46 children, avoiding either milk alone or milk and wheat, were below the average for age [71]. Another study found that, in a large sample of children, those with CMA weighed significantly less than children without milk allergies [72]. Maslin and colleagues who evaluated the diets of 13 infants on a milk-free diet against 26 healthy controls, reported that differences were found between the two groups for protein, calcium, iron, selenium, vitamin C and vitamin E intakes at differing time points, concluding that nutritional differences exist but are variable and not seen for all nutrients [73]. One study found that children with a CMA have high prevalence of iodine deficiency and poor growth [74]. Thus, avoidance of a key food group such as milk cannot only compromise the intake of obvious nutrients such as calcium, but also affects the intake of trace elements normally plentiful in the diet, such as iodine, to a sufficient degree to provoke deficiency diseases [75].

Since CMA is the most prevalent allergy amongst infants, the main nutritional goal is to ensure adequate replacement of cow's milk with suitable alternatives in non-breast-fed babies. Protein intake can be severely compromised, if substitute milks are given which do not contain sufficient protein for the infant's needs. In extreme scenarios of unsupervised food avoidance, protein energy malnutrition has led to Kwashiorkor in several children avoiding cow's milk protein [76, 77]. Venter and colleagues suggest amino acid-based formulas or extensively hydrolysed casein formulas represent the best available alternatives providing complete nutrition [58]. It has recently been shown that an amino acid-based formula is effective in providing adequate dietary mineral intake and maintaining mineral status in infants with cow's milk allergy [78]. It is important to ensure that parental perceptions regarding hypoallergenic milk substitutes do not lead to the discontinuation of standard vitamin and mineral supplements given to the child in the mistaken belief that the milk provides sufficient nutrients alone, as this can lead to low intakes of vitamin D, zinc, calcium and selenium [79]. Older children can use plant-based milks, which are usually supplemented with calcium, but may not always provide sufficient energy and protein if the rest of the diet is of poor quality or if other foods are also being avoided.

Egg allergy is another common food allergy necessitating the removal of many foods from the diet. Like milk, eggs are a highly nutritious food providing energy, protein, B vitamins and vitamin D. Vitamin D has a major role in calcium homeostasis and bone health, but also affects the innate and adaptive immune system, so supplementation is required especially for those who are not regularly exposed to sunlight. Low vitamin D levels have been associated with an increased burden of atopic dermatitis and other allergic diseases, with supplementation shown to improve atopic dermatitis in those likely to have vitamin D deficiency [1, 80]. For both milk and eggs, the emphasis in recent years has been to encourage assisted reintroduction of both foodstuffs back into the diet of allergic children, starting with baked milk and egg products [81, 82]. Many children tolerate this type of intervention, and although the introduction of baked milk and egg does not always lead to tolerance of less well-cooked milk and egg, it will help to increase variety in the diet and hence assist with the normalisation of nutritional intakes [83].

Soy allergy is usually limited to early childhood and often resolves by the age of 7 years [84]. Reactions to soy are often

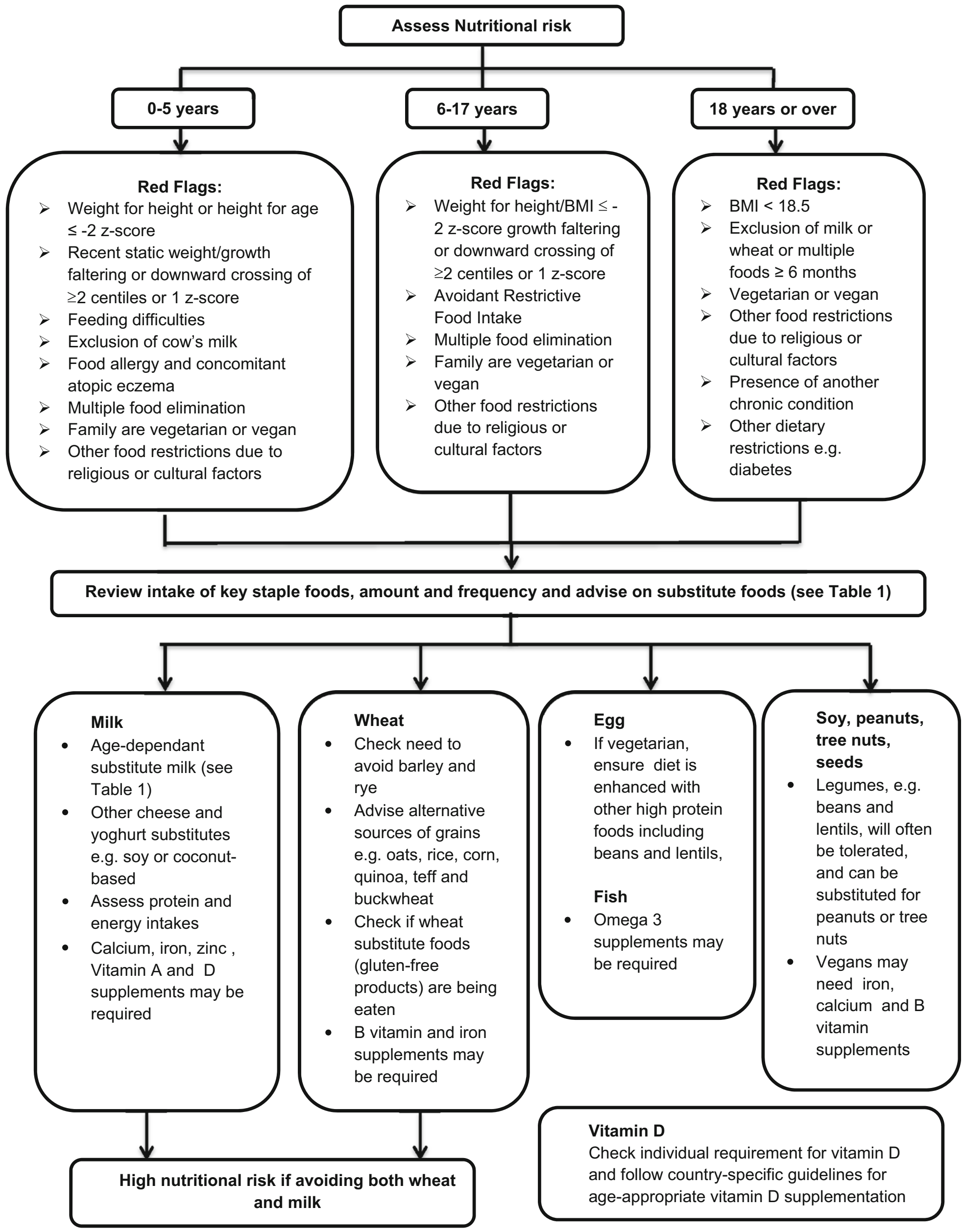

Fig. 1 Algorithm for a nutritional approach to food allergy

most problematic in non-IgE-mediated food allergy, with up to 60% of infants with non-IgE-mediated cow's milk allergy also having reactions to soy especially in enterocolitis/enteropathy syndromes [85]. Soy is often present in foods in small quantities, so the question is whether all forms of soy are equally likely to provoke symptoms. Many foods contain similar nutrients as those found in soy, so avoidance of soy alone rarely compromises the nutritional quality of the diet, but many processed foods list soy as an ingredient, which further limits choices of food-allergic individuals [73]. Wheat allergy is usually a transient allergy of childhood, but its exclusion can have a very negative effect on nutritional outcomes [86]. Wheat provides complex carbohydrates, and so is an important source of energy especially for the brain. Complex carbohydrates should provide between 45 and 65% of daily energy intake in children but cereals such as wheat also provide a unique set of micronutrients (thiamine, niacin, riboflavin, iron, folic acid) that are not found in other carbohydrate-rich foods such as fruits and vegetables [71, 87]. Thus, if grains (wheat, rye, barley, oats) are eliminated from the diet, the diet can lose a major source of complex carbohydrates, micronutrients and dietary fibre. Children following a wheat-free diet often suffer nutrient imbalance of calcium, vitamin D, iron, zinc and B-vitamins [70]. Gluten-free products often have consistently low levels of protein and other nutrients, when compared to their gluten-containing equivalents [88].

The elimination of multiple foods for diagnostic purposes can compromise the nutritional integrity of the diet. Those with eosinophilic oesophagitis (EoE), already at increased nutritional risk due to symptoms that may affect dietary intake, are often diagnosed through the elimination of six major food groups (milk, egg, wheat, soy, nuts and seafood), which provide high-quality macro- and micronutrients; thus, the diet must be time-limited to 6–8 weeks before foods are reintroduced [89].

Nutritional Issues in Adults with Food Allergy

Although growth is not a concern in adults, the elimination of staple foods has the potential to reduce the intake of vital nutrients, which in turn can affect overall health. Adults are most likely to be at nutritional risk if they are avoiding milk, wheat or multiple foods, due to suspected or actual food intolerance [90]. Food allergies in adults can either be those persisting from childhood or new-onset allergies developing in adulthood. Whilst research in children has focused on obtaining tolerance to foods, research is needed to understand why tolerance can be lost later in life.

Milk, egg, wheat and soy allergies commonly remit during childhood, although milk and egg allergy can persist into adulthood [91]. Those with persistent milk allergy face a lifetime of milk avoidance, so it is vital to ensure that there is adequate calcium in the diet to prevent bone loss. Dairy products provide a range of essential nutrients that may be lacking in the diet of those people requiring total exclusion of milk and milk products, making it difficult to achieve recommended daily calcium intakes. The skeleton is the reservoir of the body's calcium supply, which is mobilised when serum calcium levels are low; adequate calcium levels are therefore vital for bone health and muscle performance, which are closely associated with balance and fall risk in later life [92]. Bone mineral density is established by young adulthood; thus, if milk was avoided in childhood, bone health may already be compromised [70]. Poor bone health can lead to osteopenia and osteoporosis, particularly in menopausal women and the elderly. Although milk allergy in adults is rare, many adults do avoid milk due to intolerance of lactose, and adults with asthma also frequently report issues with milk [93]. Adults avoiding milk need to be made aware of the nutritional consequences and understand how to improve their intake of calcium from other sources.

It is not uncommon for nut-allergic individuals to have a lifelong allergy, although recent studies suggest remission of peanut or tree nut allergy could occur in a third or more of allergic individuals [94]. Restriction of tree nuts, legumes and seeds can have a major nutritional impact on the diet, especially for adults who are vegetarian or vegan. Seeds and nuts are a source of n-3 LCPUFA, so their removal from an already restricted diet puts these adults at nutritional risk [95]. Legumes such as soy, chickpeas, lupin and lentils are often present in bread and other foods, and seeds are also added to bakery products, limiting the dietary choices of the seed allergic individual. Legumes provide soluble fibre and protein, and nuts and seeds can enhance intakes of protein and trace minerals such as selenium. Nut consumption is associated with a reduced prevalence of raised cholesterol levels and hypertension; having a history of heart attack, diabetes and gallstones; and markers of diet quality [96].

New-onset symptoms to tree nuts, and occasionally to peanuts, presenting in adult life, are usually caused by cross-reactivity; tree pollen antibodies recognise and react to homologous proteins in tree nuts and peanuts, but also to similar allergens in raw fruits and vegetables [97]. Known as pollen-food syndrome (PFS), or oral allergy syndrome, these cross reactions usually manifest as mild oropharyngeal symptoms although concentrated amounts of allergen such as handfuls of nuts, freshly made fruit juices, smoothies or soy milk, which contains the birch cross-reacting allergen Gly m 4, can cause more severe reactions [98]. This condition usually manifests in late childhood or early adult life and can involve the exclusion of large numbers of foods from the diet. It is relatively common, affecting 2% of the UK population, especially those with allergic rhinitis [99]. Only those foods provoking symptoms need to be avoided, so PFS sufferers should be encouraged to eat those cooked fruits and vegetables which provoke symptoms when raw, and consume known cross-reactive foods if no symptoms have been previously present. From a nutritional perspective, the exclusion of some fruits, vegetables and nuts from the diet may not have a great impact, but where a large number of foods are involved, nutritional risks may occur [90]. Reducing fruit and vegetable intake could have other effects; a study by Henning et al. suggested that fruit and vegetable juices could promote beneficial changes in the intestinal microbiota [100]. Specific IgE allergy tests will often be positive for many foods in those with PFS as a result of cross-reactivity which can lead to avoidance of multiple foods due to positive tests [90, 101, 102]. It is therefore vital that PFS is correctly diagnosed, so that appropriate advice may be given on food avoidance, ensuring that nutritional aspects are not overlooked. Guidelines stress the importance of making a proper diagnosis rather than just giving patients lists of cross-reacting foods to avoid, thus preventing the needless exclusion of cross reactive fruits and vegetables [97]. It is especially important to distinguish PFS from a peanut or tree nut allergy as those with the latter diagnosis need to avoid all nuts and traces of nuts, whereas those with PFS can often tolerate cashew and pistachio nuts and also nuts in foods such as chocolates, chocolate spread, cakes, biscuits and pastries. More severe symptoms are seen in adults with another type of plant food allergy called lipid transfer protein allergy (LTP); whilst foods involved in PFS are usually tolerated if roasted or well-cooked, more severe reactions occur with LTP allergens and the foods causing reactions must be strictly avoided in all forms [103].

Wheat allergy rarely persists into adult life but can manifest in association with exercise or other co-factors [86]. As noted in children, avoidance of wheat, barley, rye and oats can lead to insufficient intake of complex carbohydrates, micronutrients and dietary fibre [70]. Adults newly diagnosed with coeliac disease may present with anaemia, vitamin B12 or folate deficiency and are additionally at increased risk of poor bone health due to impaired absorption of nutrients from damage to the small intestine [104]. But there is evidence that a gluten-free diet itself can cause nutrient deficiencies. Catassi and colleagues highlighted the fact that gluten-free diets may be low in calcium, iron, zinc, folate and fibre, affecting not only nutritional status but also the intestinal microbiota [105]. Hallert et al. found signs indicative of poor vitamin status in 56% of treated adult coeliac patients, including six on folate supplementation, suggesting that patients adhering to a strict gluten-free diet for years are prone to the development of various vitamin deficiency states, most notably folate deficiency [106]. Thus, emphasis needs to be placed on the nutritional quality of the gluten-free diet, particularly concerning iron, calcium and fibre consumption of women [107]. Adults may often avoid wheat for other reasons, and the promotion of gluten-free (GF) diets for health reasons has undoubtedly influenced this; 6.25% of adults in the Netherlands and 7.3% of Australian adults report adverse reactions to wheat [108, 109]. Many adults avoid wheat due to reported symptoms related to gluten ingestion or to alleviate symptoms related to irritable bowel disorder (IBS), but wheat avoidance may not be effective in the long term and symptoms are often not related to gluten, but possibly to other wheat components such as fructans [110, 111].

For adults, nutritional issues can arise due to lifestyle changes, and the belief that some foods such as milk and wheat are more likely to cause food allergies or intolerances. Adults who are already avoiding foods may have further nutritional compromise if they then choose to include/exclude other foods from their diet due to health reasons. Those who follow strict vegan diets can become deficient in vitamin B12 (present in milk, eggs, seafood and meat), as well as in vitamin D, zinc, calcium and iron. The risk of malnutrition is even higher in those with allergy to wheat, nuts, soy and/or other legumes as these foods are not only highly nutritious, they are the main sources of protein and energy in plant-based diets.

Discussion

Promoting the best diet during pregnancy can be difficult when supplementation with an important nutrient such as folic acid for prevention of neural tube defects may affect allergic outcomes in infants. It seems that more work is needed especially on the role of vitamin D, which out of all of the individual nutrients appears to have the most promise in terms of allergy prevention. However, it is now clear that supplementation with vitamins and minerals is less effective than promoting dietary components or particular eating patterns. Nutritional intervention for common conditions such as cardiovascular disease has led to huge changes in the composition of diets over the last 30 years, with a reduction in full fat milk and butter and increasing use of margarines. Thus, has the wheel come full circle, with the studies suggesting that milk may have a protective role during pregnancy and also in the young infant, in relation to allergic outcomes. The studies alluded to in this paper only serve to remind us that good nutrition revolves around an individualised balanced varied diet in both mother and child, and this might be the best model for allergy prevention.

Nutrition in early life has long term effects and influences the risk of chronic disease in adulthood [112]. This seems to be even more relevant for infants and young children with a food allergy. Much attention has been placed on the introduction of complementary foods in infants to prevent food allergy, but emphasis should also be focussed on encouraging diversity in the diet and promoting gut health. The biggest challenge for those working in the field of food allergy is to ensure that the nutritional quality of the diet remains strong, even when one or more foods are being excluded. All practitioners need to promote the importance of macro- and micro-nutrients and understand issues around the composition of substitute foods, especially for milk allergic children. The measurement of growth in children is a good measure of nutritional adequacy in the diet, but it should not be the only parameter, with regular assessment of other signs of deficiency. Regular dietary reviews and advice on supplementation if required are also vital; Berry et al. found that neither the type nor the nutritional quality of foods eliminated led to nutrient deficiencies if the diet was adequately supplemented [71]. Ideally, carers of the food-allergic child should receive proper counselling by a dietitian with specific competence in food allergy to help manage nutritional issues arising from food avoidance [32, 50].

For adults with a food allergy, the nutritional issues may not seem quite so obvious. However, anxiety about reactions can lead to extreme cases of restricted diets which can result not only in weight loss but also in changes to bone density. Many adults with asthma have concerns about milk and its effect on wheeze, especially those with difficult asthma who often eliminate milk from their diet [93]. Unfortunately, it is precisely this group of people who are at a higher risk of calcium deficiency and osteoporosis due to their frequent need for oral corticosteroids to gain relief from symptoms. It is a common belief that symptoms related to food are the result of a food allergy; thus, many adults attending allergy clinics will have other issues with food. On-line sources of information or social media are often used by adults to get advice about food allergy, with 85% in one study following online information which may not be from authoritative sources [113]. Enthusiastic promotion of extreme nutritional changes to the diet including the consumption of large quantities of fruit/vegetable juices or smoothies, plant ‘milks’, so-called ‘super foods’ and the avoidance of gluten can adversely affect adults with food allergies. It is vital that the allergy practitioner is aware of this and provides balanced evidence and appropriate advice and support to minimise nutritional compromise.

Conclusions/Summary

The role of food in the prevention of allergy has been well observed, but there is no clear picture yet as to the precise effects of diet on allergic outcomes either in the mother or in the infant. Thus, the main goal for the nutritional support in pregnancy and infancy should be the promotion of a healthy diet, with balanced intakes of fish, milk, eggs, cereals, fruits and vegetables, and attention paid to optimising the introduction of allergenic foods and ensuring a diverse diet. However, it is very clear that children with food allergy are at risk of growth failure, and a lack of essential nutrients which could lead to deficiency disease such as rickets and goitre. Adults can be equally at risk, especially if they are already vulnerable due to having other concomitant chronic diseases. In the allergy clinic, children, their parents and/or carers, and adults with food allergy should have access to good individualised dietary advice, to help them through the maze of internet advice. Personalised or precision medicine is the twenty-first century approach to allergy diagnosis and management; thus, an individualised approach to nutrition in every food allergic individual should be our goal.

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