

Nutritional Management of Patients With Pollen Food Syndrome: Is There a Need?

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Abstract

Purpose of review Pollen food syndrome (PFS) is a highly prevalent condition causing mild oropharyngeal reactions to plant foods due to recognition by pollen-specific antibodies. It is most frequent in adults, but it can also occur in children. This review aims to establish the pitfalls of diagnosis and the nutritional consequences, and whether individuals with PFS require an individualised dietary and nutritional management strategy.

Recent findings The diagnosis of PFS can be made through history alone but is greatly enhanced by undertaking component-resolved diagnostic (CRD) tests to individual allergens in birch pollen and relevant foods. Management of PFS requires dietary avoidance of trigger foods, but often, many foods have to be avoided, which can affect quality of life and nutritional intake. Not all symptoms are mild, especially if concentrated forms of allergen are taken, which may occur more frequently with the increased emphasis of the health benefits of fruits and vegetables. Oral food challenge (OFC) and, in the future, novel immunotherapy may minimise necessary avoidance.

Summary Due to the high homology of the allergens involved, multiple allergy tests can result in mass exclusion of antioxidant-rich fruits and vegetables, which are important nutritional contributors to the diet. Thus, those with PFS should receive individual dietary counselling to prevent deficiency diseases, especially expectant mothers, children and those who are avoiding multiple foods.

Introduction

Pollen food syndrome (PFS) is a rapid-onset food allergy that develops as a consequence of the high homology between allergens in pollens and plant foods. Depending on the pollens involved, 40–70% of sensitised individuals will develop PFS, with an estimated prevalence in the general population of over 2% [1, 2]. Manifestations usually involve mild, transient oral pruritis, but oro-pharyngeal angioedema, nausea and vomiting may occur, which can progress to wheezing or difficulty in breathing [1]. Recent evidence suggests that PFS manifestations may also include the development or increase in severity of atopic dermatitis [3•]. The main allergens involved in PFS are the pathogenesis-related (PR) 10 protein and profilin families, allergens susceptible to heat and gastric enzyme degradation [4]. Regional variations in sensitising pollens determine the type of allergen involved. The Silver Birch allergen Bet v 1 cross-reacts with PR-10 allergens and is involved in 70% of PFS reactions. Profilin allergens in mugwort, grass and ragweed pollen can also induce 50% of responses in pollen-allergic individuals [5, 6] (see Table 1). Non-specific lipid transfer protein (nsLTP) allergy is another plant food allergy, which manifests with more severe reactions and is more prevalent in the Mediterranean areas [8]. Although there are nsLTP allergens in pollens, the role of pollen sensitisation in the aetiology of nsLTP allergy is not clear and so it has not been included in this review.

Its highly typical presentation can enable a diagnosis of PFS to be made through history alone, especially if only fruits or vegetables are involved [9]. Skin-prick testing (SPT) to pollens and prick-to-prick testing to foods reported to provoke symptoms using fresh fruits, vegetables and soy milk are helpful to confirm diagnosis, as these whole foods will contain all of the allergens involved in PFS.

Component-resolved diagnosis (CRD) evaluates sensitisation to individual allergens and can distinguish between PFS and primary allergy to nuts, seeds, legumes or LTP allergens. However, broad molecular testing is not always useful, as often there is irrelevant serological cross reactivity, leading to poor positive predictive values, such as between Bet v-1 homologous Mal d 1 (apple) and Pru p 1 (peach) [10]. Testing cross-reactive allergens in peanuts and tree nuts has similar issues. The hazelnut PR10 allergen Cor a 1 is not a good predictor of allergy symptoms on challenge, and similarly, the peanut PR10 homologue Ara h8 is non-specific, but their

strong negative predictive values help rule out a diagnosis of PFS [11••, 12, 13]. In contrast, primary allergens have an increased predictive value, with Cor a 9 and Cor a 14 being highly specific for hazelnut allergy, and Ara h2 and Ara h6 good predictors of primary peanut allergy [12, 13]. A UK study found that concordance between component tests and clinical history for adults with PFS was good for hazelnut but poor for peanut [14]. Testing to Bet v 1 directly may be helpful; patients who are sensitised to birch pollen who have high levels of Bet v1 are more likely to have PFS [15]. To distinguish between PFS and possible LTP allergy, the peach LTP allergen Pru p 3 has been shown to be an effective marker, although it is not always the primary sensitising allergen [16]. Rarely, when tests and history are discordant, food provocation testing may be warranted where there is relatively low-level sensitisation to primary allergens and high levels of sensitisation to cross-reactive allergens, to understand the extent of an individual's allergic response especially with nuts. They are also useful if there is unnecessary avoidance of raw or cooked foods that do not elicit symptoms, due to fear of reactions or if there is a discrepancy between clinical history and results of skin tests or blood tests. Reduced allergenicity to cooked versions of food has been demonstrated by OFC [17, 18].

PFS is difficult to assess by OFC as often the symptoms elicited are subjective. Standardised protocols for oral food challenge do not work well with PFS involving fruits and vegetables as they are only suitable for foods with high protein contents [19]. Although attempts to standardise grading systems for subjective symptoms have been put in place, there is often bias in interpretation of results [20]. Specific protocols have been published for several PFS foods, including hazelnut [12, 21, 22], apple [9, 23], celery [17], carrot [24] and soy [25, 26]. In a recent large group study, 138 Bet v 1 and Gly m 4 sensitised patients underwent DBPCFC. A total of 45.7% presented with objective signs and 65.2% with subjective symptoms at soy challenge. In contrast, placebo challenge meals elicited objective signs in 11.6%. In 82 (59.4%) subjects, DBPCFC was judged as positive based on a scoring system of both objective and subjective signs [25]. Blinded oral food challenges (OFC) are more difficult to perform due to the unstable nature of PR-10 allergens [27] (class II). Low doses of recombinant Mal d 1 have been used as a surrogate for apple in those with PFS with no observable systemic effects [28].

Table 1. Allergens and foods involved in PFS [4–7]

	Foods predominately cross-reacting to Bet v 1				Foods predominately cross-reacting to profilins		
	Food	PR10	Profilin		Food	PR10	Profilin
Fruits	Apple	Mal d 1	Mal d 4	Fruit	Banana		Mus a 1
	Apricot	Pru ar 1			Fig		Fic c 4
	Cherry	Pru av 1	Pru av 4		Grape		
	Kiwi fruit	Act d 8	Act d 9		Kiwi fruit	Act d 8	Act d 9
	Peach	Pru p 1	Pru p 4		Melon	Cuc m 3	Cuc m 2
	Pear	Pyr c 1	Pyr p 4		Orange		Cit s 2
	Plum		Pru d 4		Pineapple		Ana c 1
	Strawberry	Fra a 1	Fra a 4			Watermelon	
Vegetables	Carrot	Dau c 1	Dau c 4	Vegetables	Aubergine		
	Celery	Api g 1	Api g 4		Carrot	Dau c 1	Dau c 4
	Tomato	Sola l 4	Sola l 1		Celery	Api g 1	Api g 4
Legumes, tree nuts and seeds	Almond		Pru du 4		Courgette		
	Brazil nut				Cucumber		
	Hazelnut	Cor a 1	Cor a 2		Fennel		
	Peanut	Ara h 8	Ara h 5		Marrow		
	Soya	Gly m 4	Gly m 3		Parsnip		
	Sunflower seed		Hel a 2		Pepper		Cap a 2
	Walnut	Jug r 5	Jug r 7		Potato		
					Pumpkin		
					Tomato	Sola l 4	Sola l 1
					Squash		
				Herbs and spices	Swiss chard		
					Angelica		
					Aniseed		
					Chilli		
					Dill		
					Caraway		
					Chervil		
					Coriander		
					Cumin		
					Mustard		Sin a 4
				Paprika			
				Parsley			

In comparison to using natural sources, the dose of Mal d1 can be standardised (ensuring constant doses) and, as the native protein is fragile, has the advantage of not being destroyed in preparation. The future use of recombinant proteins for challenge ensures consistency especially for labile proteins relevant in PFS.

Treatment

Diet and lifestyle

Nutritional strategies are vital when advising the families of children with multiple allergies, especially when avoiding staple foods, such as milk, egg or wheat [29]. By contrast, the majority of PFS is diagnosed in adults, and the foods excluded are usually fruits and vegetables, thus dietary avoidance is often seen as relatively straightforward. However, if no authoritative information is provided, the majority of adults will refer to and often follow sources of online information, which may be misleading [30]. The increased promotion and consequent consumption of “superfoods”, juices, smoothies and soy protein shakes, which may contain concentrated PR-10 allergens, could provoke severe reactions [31]. Guidelines stress the importance of making a proper diagnosis rather than just giving patients lists of cross-reacting foods to avoid [17]. New evidence suggests that those with PFS who have multiple relevant food allergies have a greater impairment of health-related quality of life (HRQL) [32•] (class II). A study on 73 patients with a history of PFS provided information on triggers and symptoms in addition to completing questions from a validated food allergy quality of life questionnaire; women, older people and those affected by multiple food triggers had a greater impairment of HRQL. Therefore, if multiple foods are being avoided, dietary counselling is vital, but also establishing tolerance to foods where sensitisation rather than allergy is suspected and using interventions, such as oral food challenge, if required [27].

Nutritional and dietary issues

The literature pertaining to nutritional inadequacy in adults with food allergy is sparse. In atopic dermatitis, it has been demonstrated across the age range that avoidance of three or more foods was associated with nutritional deficiencies [33]. Case reports have shown that extreme avoidance of plant foods can lead to deficiency diseases, such as scurvy, and the health benefits of fruits and vegetables are such that even moderate avoidance should be nutritionally reviewed [34, 35]. Other considerations include the benefits of fruits and vegetables in the maternal diet; higher pre-natal intakes of total fruit and vegetables have been associated with a decreased risk of respiratory tract infections in offspring [36] (class II). Those with PFS who are vegetarian or vegan will be at the highest nutritional risk, especially if they are avoiding tree nuts and peanuts as this will severely impact on their intake of protein, omega 3 and 6 fats and trace nutrients, such as selenium [37] (see Table 2). Increasing intakes of nuts and seeds which are tolerated will help to maintain good intakes of protein, polyunsaturated fats, and trace minerals, and may help to reduce the risk of hypercholesterolemia, hypertension, diabetes and gallstones [38] (class II). This is again especially important in those eating a purely plant-based diet, as nuts and seeds often provide the main sources of energy, protein, fibre, B vitamins and calcium.

Table 2. Nutrients in plant foods and substitutes for individual foods

Food trigger	Nutrients provided	Foods to avoid	Substitute foods
Peanuts	Protein, magnesium, calcium, vitamin B6, niacin	Monkey nuts, raw peanuts, peanut bars	Roasted or boiled peanuts and peanut butter may be tolerated. If not, cashew or edamame beans may be a snack substitute. For peanuts in foods, roasted or ground almonds or cashew nuts may be a good substitute. Peanuts in foods may be tolerated, but peanut butter or peanut-containing chocolates may not be. No need to avoid foods "stating may contain nuts"
Almonds	Protein, polyunsaturated fat, calcium, magnesium, phosphorus, folic acid	Raw almonds, raw nut bars, muesli or cereals with a lot of raw nuts	Blanched almonds (with brown skin removed) may be tolerated. Almonds in foods including marzipan, frangipane, cakes, biscuits, chocolates, savoury foods such as curry should be tolerated. Seeds are a good substitute for nuts, such as pine nuts and pumpkin seeds. Avocado and vegetable oils are good sources of fatty acids.
Hazelnuts	Protein, calcium, magnesium, vitamin E, folic acid	Raw hazelnuts, raw nut bars, muesli or cereals with a lot of raw nuts	Blanched hazelnuts (with brown skin removed) may be tolerated. Hazelnuts in chocolates, chocolate spread, cakes, biscuits, pastry, desserts
Brazil nuts	Protein, polyunsaturated fat, selenium, calcium, magnesium, phosphorus	Raw Brazil nuts	Brazil nuts in chocolate may be tolerated providing they are not whole.
Walnuts	Protein, polyunsaturated fat, magnesium, phosphorus, folic acid	Raw walnuts, raw nut bars, muesli or cereals with a lot of raw nuts	Walnuts in foods including chocolate, cakes, biscuits, baked desserts.
Cashew and pistachio nuts	Protein, calcium, iron, magnesium, folic acid	None—these foods should be tolerated	Useful to substitute for other nuts and also for peanuts, both as a snack and also in sweet and savoury foods.
Fruits and vegetables	Fibre, antioxidants and a variety of vitamins and minerals including B vitamins (folic acid, thiamine, riboflavin), vitamin C, β -carotene,	Smoothies and fresh fruit or vegetables juices, unless made at home with known tolerated fruits or vegetables	Only the raw fruits and vegetables that provoke symptoms should be excluded. Foods which have been peeled, or microwaved or cooked may be tolerated. Suggest try different varieties

Table 2. (Continued)

Food trigger	Nutrients provided	Foods to avoid	Substitute foods
	calcium, iron and magnesium		of the same fruit, as different varieties may be tolerated. Also, larger tomatoes, which can be peeled and the pips removed may be better tolerated than smaller varieties of tomatoes such as cherry tomatoes which contain more pips and peels.
Soy and other legumes	Energy, protein, fibre, B vitamins, calcium, magnesium, iron and zinc	Soy milk, edamame beans, whole cooked soy beans, soy protein shakes, soy protein bars	Whole grain cereals can provide a good variety of the nutrients provided by soy and other legumes. So, it is important to increase the amount of whole grains in the diet if soy and other legumes are being excluded. Those with PFS usually only need to avoid concentrated sources of soy. Fermented soy products and foods containing soy flour should be tolerated, e.g., soy sauce, tofu, bread, sausages, biscuits, cakes

Typically, the dietary restriction with PFS often means a large number of fruits and vegetables may need to be excluded. Such restrictions may impact on their ability to achieve national targets for the consumption of fruits and vegetables; however, one small study reported that 62% of those with PFS achieved the UK 5-a-day target compared to 53% of those with spring hay fever but no PFS, suggesting PFS does not impact on an individual's ability to achieve the 5-a-day target [39]. The nutritional value of the diet may also be compromised due to the need for those with PFS to cook many fruits and vegetables in order to be able to consume them. This may cause the loss of water-soluble vitamins, such as thiamine (B1), riboflavin (B2), folic acid and vitamin C, which can leach out into cooking water. It has been shown that microwaved vegetables retain the most vitamin C compared to those that are steamed or boiled [40]. To improve nutritional intake in PFS, OFC can also play a vital part in demonstrating tolerance to related foods and cooked versions of the food and clarify the diagnosis and the relevance of cross-sensitization [41].

Dietary management

In order to maximise the number of foods in the diet, it is vital to establish pollen sensitisation patterns, so patients can be advised which foods might be well-tolerated, especially if they are avoiding a large number of foods (see

Table 1). One complicating factor in PFS management is whether the patients should exclude foods containing homologous PR-10 or profilin allergens or botanical relatives of the offending trigger food(s). There is no evidence that this is advisable as the natural history of PFS is poorly understood, and despite homology, patients can often tolerate a large number of cross-reactive foods. Peanuts and tree nuts contain both PR-10 proteins and profilins, and thus, SPT and CRD might be positive in individuals sensitised to tree or grass pollen, but without relevance [42•] (class II).

Strict avoidance of foods has been linked to increased anxiety, especially to nuts. In a large observational cohort study of 785 patients, 85% of whom were declared allergic, anxiety was significantly associated with strict avoidance ($P < 0.001$) [43•] (class II). Thus, it is important to make sure that the avoidance of peanuts and tree nuts in those with PFS is proportionate compared to primary peanut allergy. Roasted nuts may be tolerated as PR-10 homologues in tree nuts and peanuts, such as Ara h 8 and Cor a 1, have been shown to have a low stability to roasting, although their activity is not fully curtailed, so these foods might still provoke symptoms [44, 45]. Foods containing nuts or with labels stating they “may contain nuts” are usually tolerated. It is important that this is comprehended by the patient, as avoiding all nut-containing foods severely restricts food choice and in many instances foods with labels bearing advisory nut statements are often free from nut contamination [46]. Symptoms may also be minimised in composite foods due to the matrix effect, which can alter the allergenic effects of a food [47]. Pistachio and cashew nuts are generally tolerated and, apart from sunflower seeds, other seeds, such as sesame seeds, pumpkin seeds and pine nuts, are not noted to be involved in the PFS spectrum [48]. Apart from peanuts, other legumes, such as soy, predominantly in the form of soy milk, is one food that has been shown to provoke severe PFS reactions due to a high level of the PR-10 allergen Gly m 4 [31]. One study reported that 15/20 patients who had reactions to fruits and vegetables also had reacted to soy drinks [49]. However other forms of soy, which are found in a wide range of foods including bread, pastry products and meat products, are usually tolerated.

Fruits or vegetables may be easy to avoid if only one or two are involved. However, one study found that the average number of foods being avoided in PFS was four, and patients may be symptomatic to many more, especially if poly-sensitised to grass, tree and weed pollens [2]. Raw vegetables may not always be easy to exclude, being often used as garnishes or added to salads or stir-fry meals which may not be cooked sufficiently to denature the PR10 proteins. Often, patients with multiple allergies to fruits and vegetables may wish to consume novel foods or those which are not traditional to the native diet of that country. However many “tropical” fruits may provoke reactions; severe reactions to jackfruit are linked to latex allergy, but jackfruit does also cross-react with birch tree pollen and so may cause reactions in individuals sensitised to birch rather than latex [50, 51]. Other non-traditional pollen cross-reacting foods include tiger nuts [52].

Patients should be advised to try different varieties of fruits or vegetables as there are low-allergen varieties which may be tolerated [53]. Bolhaar and colleagues undertook skin-prick testing with 21 apple cultivars DBPCFC with Golden Delicious and Santana apples and reported a significant difference in allergenicity between them [54]. Other studies have shown similar results,

suggesting that Golden Delicious, Granny Smith, Starking and Cox's Orange Pippin apples are more likely to provoke symptoms, whereas low-allergen apple cultivars, such as Royal Gala, may be tolerated [55, 56]. Another study evaluating data from 46 adults with birch pollen allergy underwent SPT to 11 apple cultivars; those with PFS had more positive responses, especially the apple cultivars Szara Reneta and Cortland, compared to those who had birch pollen allergy but no PFS [15]. However, low-allergen apples do not always prove to be better tolerated. Sixty-six individuals with PFS to apples underwent double-blind oral provocation to two different apple cultivars, a low allergen cultivar, B:0654 and "Discovery" apples. The authors reported that the low allergen apple induced significantly higher symptom scores than "Discovery" even though B:0654 had a lower level of the apple Bet v 1 homologue Mal d 1 [57]. One reason for designated low-allergen apples still provoking symptoms may be due to the presence of other allergens which can also provoke symptoms. In addition to their work identifying the levels of Mal d 1 in apples, Sancho and colleagues also found there to be great variation in the amount of Mal d 3 in different varieties, there being up to a 100-fold difference in the level of Mal d 3 between cultivars, with 53 cultivars from Italy and 35 from the Netherlands [58].

Storage of foods may also affect the amount of allergen. Storage has been shown to increase Mal d 1 and as such freshly picked apples may be better tolerated in PFS [59]. The same group reported that during maturation on the tree, the level of Mal d 3 increases, but during storage, the level subsequently decreases especially under controlled atmosphere conditions [60]. Despite suggestions that organic fruits and vegetables may be less allergenic, as compared to those grown using conventional methods, a study analysing the level of profilin, PR10 proteins and nsLTP allergens in tomatoes from both organic and conventional systems over three consecutive years, concluded that organically grown tomatoes are no less allergenic [61]. Varietal differences in levels of allergen, effects of maturation and storage on allergen levels make it vital to ensure the correct diagnosis is reached for patients with symptoms to apple. Peeling may improve tolerance; since the peels of the fruits will contain more of the allergen, and microwaving may be sufficient to alter the PR10 allergens [62].

Apart from varietal differences in raw fruits, advice is often predicated on the fact that all cooked foods provoking PFS are tolerated. This fact may be utilised to distinguish between PFS and LTP allergy, as typically LTP allergens are not affected by heat [63]. Although many Bet v 1 homologous PR10 proteins are highly susceptible to heat and degradation, cooking methods may vary in their effect on the allergens, and some allergens are resistant to heat. A review by Pekar and colleagues reported that thermal processing affects the food matrix [64••]. The Maillard reaction involves protein glycation, but the glycation of fruit allergens does not always have the same effect on the allergenicity of the food [65]. The IgE-binding capacity of PR10 allergens is decreased whereas it appears that the LTP allergens appear to be protected [51, 66].

Sancho and colleagues evaluated the impact of digestion by pepsin on the IgE-binding activity of rApi g 1 (celery), rMal d 1, rPru p 1 and rCor a 1 and found rApi g 1 to be the most stable [67]. The celery Bet v 1 homologue typically can cause severe reactions, and this may be due to its ability to withstand heat and gastric degradation. Ballmer Webber and colleagues demonstrated that 6/11 patients showed a positive DBPCFC to cooked celery, demonstrating

reactivity to both Api g 1 and Api g 4 [68]. A recent study on the stability of Api g 1 found that it was not susceptible to heat but did report susceptibility to pH, so the type of processing may affect how allergenic the celery component of a composite food will be [69].

Although digestion or cooking diminishes or eliminates immediate IgE-mediated reactions, it does not affect T cell cross-reactivity, and the consumption of pollen-related food allergens stimulates pollen-specific T cells to exert effector functions [70]. Fresh birch pollen-related foods have been shown to activate peripheral Bet v 1-specific T cells to migrate to the skin and mediate late-phase eczematous reactions [71, 72]. In addition, 32/65 adults and children with atopic dermatitis challenged with birch pollen-related foods had a significant increase of symptoms and rise in clinical atopic dermatitis scoring [3•].

There is very little evidence assessing the reactivity of PR10 allergens in relation to freezing, although one study assessing the allergenic properties of frozen fresh fruits for the purposes of skin-prick testing concluded that the fruits were unaffected, so it is possible that frozen apples or other soft fruits may still provoke symptoms [73].

Pharmacologic treatment

The evidence basis for current medical management of PFS is weak, often from poorly powered and non-randomised studies. The long-acting H1 antihistamine astemizole given regularly prophylactically was able to diminish but not abolish symptoms on exposure in PFS [74]. Prophylactic antihistamines are not recommended for food allergy, and in case of severe reactions, anti-histamines may mask early severe symptoms and delay treatment [75]. There is no evidence for the use of mast cell stabilisers in the treatment of PFS. The benefits of specific H1 antihistamines over others have not been reported, and the safety profile of use in food reactions is not well-characterised.

Adrenaline auto-injectors (AAI) are recommended for acute severe reactions to food [7]. There is significant discrepancy in the rates of prescription of AAI for PFS globally and no studies on whether it is necessary or beneficial. In two large survey studies, in the UK, 13% of allergy practitioners would prescribe them in comparison to 70% of practitioners in the United States [76, 77]. Concomitant allergic rhinitis and asthma treatment should be optimised in PFS though there is no evidence that this will improve related symptoms. To our knowledge, the specific costs for PFS medical treatment have not been evaluated.

Emerging therapies

Attempts to treat PFS with allergen immunotherapy to the sensitising pollen have been undertaken with conflicting results. Subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) with whole and recombinant allergens have been trialled. In a trial of 25 patients randomised to birch pollen SCIT or medical management, patients on SCIT were able to tolerate an increased apple dose by a factor of 24 judged by DBPCFC after 1 year of immunotherapy [78]. Other studies have shown similar results [79]. Several larger trials have refuted these results with no clinical effect seen [80–82]. Despite the homology between allergens, birch pollen immunotherapy decreased specific IgE and T cell reactivity to Bet v1, but similar responses were not seen to Mal d 1 [82]. These studies have predominantly looked at the effect

of 1 year of immunotherapy and immediate induction of tolerance rather than long-term effects. Currently, birch pollen immunotherapy is not recommended for PFS [27].

As evidenced by the minimal effect of birch pollen immunotherapy, the specificity of the allergen used in immunotherapy to induce tolerant immune responses may be vital. Recently, several trials involving recombinant Bet v1 immunotherapy have been used in immunotherapy for PFS. In a trial on soy PFS, 82 Bet v1 sensitised patients allergic to soy had 1 year of recombinant Bet v1 SLIT. On DBPCFC looking for tolerance to soy, statistical significance compared to placebo was not reached, though immunological changes including a rise in specific IgG4 against Gly m4 were seen [83]. Recombinant Mal d1 has also been used directly as immunotherapy. In a pilot study comparing Mal d1 to recombinant Bet v1 immunotherapy, Mal d1 immunotherapy was significantly more effective than Bet v1 in inducing tolerance to both a Mal d1 challenge and apple tolerance [84•]. Recently, a hybrid protein has been created with Bet v1 plus T cell-reactive epitopes from Mal d1 and Cor a1 to make a molecule that induces immune responses to give a widespread response to birch pollen and associated food allergies though this has only been trialled in murine studies [85]. A non-placebo controlled study found that 17/27 patients with PFS could achieve tolerance of a whole apple by eating regular increasing amounts of apple on a daily basis for 8 months [86].

Initially, it was thought that recombinant therapies may improve safety and efficacy of immunotherapy, but this has not been demonstrated when using recombinant Bet v1 versus whole birch immunotherapy [87]. Most side effects in trials of immunotherapy for PFS have been local and mild affecting up to 60% of participants [83].

Paediatric considerations

This condition was once considered to be a disease of adulthood. However, recent studies from Italy, UK and Spain all suggest that children as young as 6 years old can develop PFS [88–90]. The diagnosis and management are the same as for adults, but there should be a special emphasis on ensuring an accurate diagnosis to ensure that there is no nutritional compromise.

Conclusion

Pollen food syndrome is a highly prevalent food allergy occurring predominantly in adult life, manifesting in mild oro-pharyngeal symptoms due to cross-reactivity between pollens and plant foods. Diagnosis of PFS is achieved through clinical history and standard allergy testing, although the highly homologous nature of the allergens involved can result in a large number of positive tests. Thus, molecular allergy diagnosis can be extremely helpful in determining the true meaning of test results, especially to nuts. The current mainstay of treatment for PFS is avoidance of causative foods; unfortunately, the large number of potential cross-reacting foods can result in symptoms to and the exclusion of many fruits, vegetables and nuts. An oral food challenge can be helpful in confirming the relevance of positive tests to both improve diagnosis and minimise food avoidance.

The evidence for the degree of avoidance and the subsequent nutritional implications is limited, and further research is needed in both adult and paediatric populations. The restricted diet of the PFS sufferer can adversely affect nutritional adequacy, especially in those already avoiding other key food groups, such as vegetarians or vegans. There can also be a noticeable effect on quality of life when multiple foods are excluded. Novel therapies such as immunotherapy show some promise in improving tolerance, although at present, there is insufficient evidence to justify their widespread use. Allergists and allergy dietitians play an important role in ensuring patients receive the correct diagnosis and nutritional management, to minimise food avoidance until cure may be achievable in the future.

Compliance with ethical standards

Conflict of interest

Natasha Gunawardana declares that she has no conflict of interest. Helena Rey Garcia declares that she has no conflict of interest. Isabel Skypala declares that she has no conflict of interest.

Human and animal rights and informed consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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- Of importance
- Of major importance

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