



## Review Article

## Review Article: Pollen food allergy syndrome (PFAS): A review of current available literature

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## Key Messages

- Prevalence of pollen food allergy syndrome (PFAS) varies by geographic location and is between 2% and 70% based on the study.
- Pollen food allergy syndrome can presents as a spectrum of symptoms ranging from isolated oropharyngeal symptoms to anaphylactic shock.
- Treatment of PFAS needs to factor in risk of severe reaction, quality of life, cost, and patient preference.
- Risk assessment will be able to be more individualized as additional component testing becomes available.

## ARTICLE INFO

## Article history:

Received for publication June 11, 2019.

Received in revised form July 16, 2019.

Accepted for publication July 24, 2019.

## ABSTRACT

**Objective:** Pollen food allergy syndrome (PFAS) is a complex syndrome posing a diagnostic and therapeutic challenge. Our objective was to summarize the available literature regarding its prevalence, pathogenesis, diagnosis, and treatment.

**Data Sources:** A PubMed search was performed to include English language articles with the following search terms: *pollen food syndrome, pollen food allergy syndrome, PFAS, oral allergy syndrome, OAS, food anaphylaxis, food components*.

**Study Selections:** Human articles discussing PFAS.

**Results:** Varying reports have been made of the prevalence of PFAS, ranging from 4.7% to greater than 20% in children and 13% to 58% in adults. Prevalence varies widely by geographic region. PFAS is typically the results of class II food allergens (e.g. sensitized to anaeroallergen, but reaction occurs due to cross reactivity from a food allergen). Commonly these reactions are limited to the oropharynx due to the lability of the proteins causing the reaction. As multiple families of proteins with varying stability cause PFAS, severe systemic reactions are also possible, as anaphylactic shock has been documented in up to 1.7% of reactions.

**Conclusion:** Pollen food allergy syndrome therefore cannot be dismissed as a benign food allergy, but it needs to be approached individually based on known risk factors.

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## Introduction

Although first descriptions of this syndrome date back as far as 1942,<sup>1</sup> the term *oral allergy syndrome* (OAS), first proposed in 1987, was used to describe the symptoms of allergies to various foods in aeroallergen-allergic patients.<sup>2,3</sup> In 1995, the term *PFAS* (pollen food allergy syndrome) was used to better characterize the

pathogenesis and avoid confusion as to possible symptoms.<sup>4</sup> It has been used primarily as an overarching term for several described entities such as birch-pollen, mugwort-celery-spice, and ragweed-melon syndromes.

If we define food allergies per the 2010 US guidelines as “an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food,”<sup>5</sup> then all these reactions qualify as food allergies. Even so, clearly these reactions are different from what is commonly thought of as a “food allergy.” One paradigm of approaching this is by using class I vs class II food allergens. Class I are food allergens in which the sensitization

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**Disclosures:** none.

**Funding Sources:** none.

<https://doi.org/10.1016/j.anai.2019.07.022>

1081-1206/Published by Elsevier Inc. on behalf of the American College of Allergy, Asthma & Immunology.

occurs through the gastrointestinal (GI) tract from a protein resistant to digestion, and class II food allergens are caused by prior sensitization to an aeroallergen and cross-reactivity.<sup>6</sup> By thinking of PFAS as class II food allergens and not as a syndrome described with only oral and perioral symptoms, it is easier to conceptualize why this disease presents the way it does.

## Prevalence

A recent study by Gupta et al<sup>7</sup> reports the prevalence of food allergy to be 10.8% in a population-based survey of more than 40,000 US adults.<sup>7</sup> In some other studies, PFAS has been excluded from calculating “food allergy” prevalence, as shown in the paper by Kamdar et al,<sup>8</sup> because they have in their exclusion criteria “a history consistent with oral allergy syndrome.”<sup>8</sup> Often the prevalence of PFAS is reported as the percentage of another disease, such as “10% of children with allergic diseases develop OAS.” Other examples include: 20% to 70% of persons with pollen allergy experience pollen-related food allergy; approximately 20% of patients who underwent skin prick testing experience PFAS; 45% of patients with seasonal allergies reported PFAS; and 26% to 34% of patients with eosinophilic esophagitis have PFAS.<sup>9–13</sup>

Studies that are trying to determine the prevalence of PFAS often get their starting population from those with allergic rhinitis or patients with known sensitivities to aeroallergens associated with PFAS, leading to the potential of falsely elevated prevalence rates. Rates between 4.7% and more than 20% have been reported in children, and 13% to 53.8% in adults.<sup>14–18</sup> In a UK survey conducted in 3590 subjects, an average prevalence of 2% was found, ranging from 0.8% to 4.1%, depending on the area within the survey.<sup>19</sup> In a smaller study of 173 subjects ages 18 to 24 from the general population of Armenia, the prevalence was found to be 13%.<sup>20</sup>

The prevalence also is known to vary according to geographic location, because of the aeroallergens in that location and their likelihood to cause class II food allergy. In areas endemic with birch, PFAS is estimated to affect 50% to 90% of birch-allergic patients.<sup>19–21</sup> Another way of estimating the prevalence is to determine the percentage of the population affected by the disease that the subpopulation studied is taken from. In other words, given that allergic rhinitis affects between 20% and 50% of the population and 47% to 70% of patients with pollen allergy experience PFAS,<sup>22–24</sup> the estimated prevalence would be calculated as being between 9.4% and 35%. Although the true prevalence will be difficult to determine given the wide geographic variability, it does affect a significant portion of the population. Appropriate recognition, diagnosis, and management is therefore an essential skill for a practicing allergist.

## Symptoms

Although commonly thought of as a low-risk disease, up to 3% of patients with PFAS experience systemic symptoms without oral symptoms, and 1.7% experience anaphylactic shock.<sup>25</sup> The most common symptom is oral-pharyngeal pruritus.<sup>26</sup> Other symptoms include tightness in the throat, difficulty swallowing, nausea, dysphonia, nasal itching, and itching of the ear.<sup>17,27–29</sup> Often these symptoms occur only when eating the raw food, and the patient may tolerate cooked/processed foods. Other factors that affect protein degradation may affect the occurrence or severity of a reaction such as anti-acid medication, which may cause decreased protein degradation and therefore increased reaction rate or severity. Volume of food ingested and exercise affect both class I food allergies and class 2 food allergies. During an acute episode of PFAS, physical examination may reveal several features, such as angioedema of the tongue, uvula, lips, face, and periorbital area, as well as perioral urticarial eruptions.<sup>29–34</sup> The symptoms present are typically localized to the area around the beginning of the GI

tract. Reports have been made of systemic or severe features, which include urticaria, dyspnea, and even anaphylactic shock.<sup>35,36</sup> Indeed, certain foods have been implicated for a higher risk of anaphylaxis in class II food allergies. These foods include almonds, apricots, cherries, celery, lentils, peaches, plums, and tomatoes.<sup>3,29,36–40</sup> Several explanations exist that help to conceptualize why certain foods may increase the risk of systemic reactions while others do not. A look into the underlying pathogenesis can shed light on the varying presentations observed.

## Pathogenesis

When looking at PFAS, the primary concern is class II food allergens. The food allergen itself is not typically the primary sensitizer, as would be seen in class I food allergens. In general, class I food allergens are heat and digestion stable. By remaining stable, they are able to retain their immunoglobulin E (IgE)-binding conformation, potentially leading to an increased ability to sensitize and a higher incidence of severe systemic reactions.

Most (approximately 65%) plant food allergens (both class I and class II) belong to 3 classes of protein superfamilies: the prolamin superfamily; the cupin superfamily, and the pathogenesis-related (PR) proteins family.<sup>41,42</sup> Given the immense size of the prolamin family, they have been broken up into 2S albumins and lipid transfer proteins (LTP) for this review.

Lipid transfer proteins are pan-allergens found in many fruits and vegetables that are resistant to both heat and digestion. A Mal d 3 (apple) LTP maintains IgE reactivity despite thermal treatment (90°C, 20 minutes).<sup>43</sup> Severe LTP-induced reactions are seen in individuals who do not have sensitization with the labile allergens such as PR-10 (ie, co-sensitization with PR-10 proteins appear to be a protective factor).<sup>44</sup> The reason for this is not known. In a study of LTPs by Palacin et al,<sup>45</sup> a microarray immunoassay was performed that suggested that LTP from Pru p 3 (peach) acts as a primary sensitizer and is the main gateway to polysensitization of LTPs.<sup>45</sup> Another study by Schulten et al<sup>46</sup> showed that Pru p 3 was the cause of sensitization to Cor a 8 (hazelnut).<sup>46</sup>

In a study of LTP allergy using a multiplex diagnostic array, most patients that are LTP allergic recognize more than 6 LTPs, with Pru p 3 and Mal d 3 being the most common.<sup>47</sup> Other relevant examples of LTPs include Ara h 9 (peanut), Gly m 1 (soybean), Jug r 3 (walnut), and Tri a 14 (wheat). A comprehensive list of allergen LTPs is shown in Table 1. The LTPs have significant binding to lipid molecules, which may help protect them from degradation.<sup>48</sup> Lipid binding is common to both class I and class II allergens.<sup>49</sup>

The 2S albumins are also members of the prolamin superfamily and have a limited role in PFAS. No identified aeroallergen that is a 2S albumin has been found that could act as a primary sensitizer. Thus, any identified 2S albumins (eg, Ara h 2 [peanut] and Ana o 3 [cashew]) suggest a class I allergen. Some overlap is seen with the cupins in their function, because 2S albumins and 7S and 11S are all considered storage proteins, as discussed further. A list of these components is given in Table 2.

The cupin superfamily contains an extremely diverse group of proteins. It includes multiple proteins of various functions as well as seed storage proteins (7S and 11S), which are the most relevant to allergy. The term *cupin* is derived from the Latin term *cupa*, referring to the conserved barrel domain found in this group of proteins. The most relevant proteins to our discussion in this family include Ara h 1 and 3 (peanut), Jug r 2 (walnut), Ses i 3 (sesame seed), Ber e 2 (brazil nut), and Cor a 9 (hazelnut).<sup>48</sup> Patients are often sensitized to these class I allergens, and similar to the other storage protein 2S albumin, no identified 7S or 11S aeroallergens would function as the primary sensitizer. Table 3 shows components identified as cupins, suggesting that they would represent a class I food allergy.

**Table 1**

A compilation of LTP components for foods and aeroallergens

| Prolamin (LTP)           |          |                |                    |
|--------------------------|----------|----------------|--------------------|
| Aeroallergen             | Foods    |                |                    |
| Indian hemp              | Can s 3  | Almond         | Pru du 3           |
| London plane tree        | Pla a 3  | Apple          | Mal d 3            |
| Mugwort                  | Art v 3  | Apricot        | Pru ar 3           |
| Oriental plane           | Pla or 3 | Asparagus      | Aspa o 1           |
| Para rubber tree (latex) | Hev b 12 | Banana         | Mus a 3            |
| Short ragweed            | Amb a 6  | Cabbage        | Bra o 3            |
|                          |          | Celery         | Api g 2, 6         |
|                          |          | Cherry         | Pru av 3           |
|                          |          | Chestnut       | Cas s 8            |
|                          |          | Grape          | Vit v 1            |
|                          |          | Green bean     | Pha v 3            |
|                          |          | Hazelnut       | Cor a 8            |
|                          |          | Kiwi           | Act c 10, Act d 10 |
|                          |          | Lemon          | Cit l 3            |
|                          |          | Lentil         | Len c 3            |
|                          |          | Lettuce        | Lac s 1            |
|                          |          | Mulberry       | Mor n 3            |
|                          |          | Olive          | Ole e 7            |
|                          |          | Orange         | Cit s 3            |
|                          |          | Pea            | Pis s 3            |
|                          |          | Peach          | Pru p 3            |
|                          |          | Peanut         | Ara h 9, 16, 17    |
|                          |          | Plum           | Pru d 3            |
|                          |          | Pomegranate    | Pun g 1            |
|                          |          | Raspberry      | Rub i 3            |
|                          |          | Strawberry     | Fra a 3            |
|                          |          | Sunflower      | Hel a 3            |
|                          |          | Tangerine      | Cit r 3            |
|                          |          | Tomato         | Sola i 3, 6, 7     |
|                          |          | Walnut         | Jug r 3            |
|                          |          | Wheat          | Tri a 14           |
|                          |          | Yellow mustard | Sin a 3            |

The PR family plays a large role in PFAS. Perhaps the most prominent of these is PR-10. One of the best studied of these proteins is Bet v 1 (birch). The development of the PR proteins were a protective mechanism against pathogenic invasion. These proteins can be found among many plant species.<sup>29</sup> The PR proteins are also formed in response to various stresses, such as mechanical trauma, drought, or flooding.<sup>50</sup> Some of the relevant members of this family include Mal d 1 (apple), Pru av 1 (cherry) Pru ar 1 (apricot), Pyr c 1 (pear), Api g 1 (celery), Dau c 1 (carrot), Gly m 4 (soybean), Cor a 1 (hazelnut), and Ara h 8 (peanut).<sup>51</sup> A more comprehensive list of PR proteins is given in Table 4. This group is thought to be primarily class II food allergens.<sup>52–54</sup> Unlike LTPs, these Bet v 1 homologs are more labile and thus are less likely to be able to cause primary

**Table 2**

A compilation of 2S albumins components for foods and aeroallergens

| Prolamin (2S albumins) |                         |                  |  |
|------------------------|-------------------------|------------------|--|
| Aeroallergen           | Foods                   |                  |  |
| None                   | Brazil nut              | Ber e 1          |  |
|                        | Buckwheat               | Fag e 2, Fag t 2 |  |
|                        | Cashew                  | Ana o 3          |  |
|                        | Castor bean             | Ric c 1          |  |
|                        | Field mustard/turnip    | Bra r 1          |  |
|                        | Hazelnut                | Cor a 14         |  |
|                        | Indian/oriental mustard | Bra j 1          |  |
|                        | Kiwi                    | Act d 13         |  |
|                        | Peanut                  | Ara h 2, 6, 7    |  |
|                        | Pecan                   | Car i 1          |  |
|                        | Pistachio               | Pis v 1          |  |
|                        | Pumpkin                 | Cuc ma 5         |  |
|                        | Rapeseed                | Bra n 1          |  |
|                        | Sesame                  | Ses i 1, 2       |  |
|                        | Soybean                 | Gly m 8          |  |
|                        | Stone pine (pine nut)   | Pin p 1          |  |
|                        | Walnut                  | Jug n 1, Jug r 1 |  |
|                        | Yellow mustard          | Sin a 1          |  |

**Table 3**

A compilation of Cupin components for foods and aeroallergens

| Cupins       |                |               |  |
|--------------|----------------|---------------|--|
| Aeroallergen | Foods          |               |  |
| None         | Almond         | Pru du 6      |  |
|              | Brazil nut     | Ber e 2       |  |
|              | Hazelnut       | Cor a 9, 11   |  |
|              | Kiwi           | Act d 12      |  |
|              | Peanut         | Ara h 1, 3    |  |
|              | Pistachio      | Pis v 2, 5    |  |
|              | Pumpkin        | Cuc ma 4      |  |
|              | Sesame         | Ses i 3, 6, 7 |  |
|              | Soybean        | Gly m 5, 6    |  |
|              | Walnut         | Jug r 4       |  |
|              | Yellow mustard | Sin a 2       |  |

sensitization. The lability of these proteins means that they often become denatured with cooking, or processing of foods. Being able to tolerate processed foods, but having symptoms to fresh foods, is highly suggestive of PFAS.

Profilins, another family of proteins, share some characteristics with the PR-10 proteins. They are easily degraded by gastric digestion, and thus there is a reduced chance of a reaction progressing beyond oral symptoms.<sup>55</sup> Profilins share significant homology amongst themselves. Because of this homology, between 20% and 30% of all patients with tree pollen allergy react to profilins, and sensitization with profilins is associated with multiple pollen-associated food allergies.<sup>37,56–58</sup> Relevant profilins include Ana c 1 (pineapple), Api g 4 (celery), Ara h 5 (peanut), Dau c 4 (carrot), and Cor a 2 (hazelnut). Table 5 gives a more comprehensive list.<sup>59</sup>

### Cross-reactivity

As mentioned previously, many syndromes under the PFAS umbrella exist. These syndromes are typically named based on describing what cross-reactivity is observed. Some of the most clinically relevant of these are described here. Tables 1 through 5 provide a fairly comprehensive list of possible cross-reactivities.<sup>59</sup> A more clinically focused list adapted from Ramesh and Lieberman<sup>60</sup> is shown in Table 6. Sensitization to birch has been shown to be cross-reactive to multiple fruits, vegetables, and nuts.<sup>51</sup> Which foods individuals react to depend on which component of birch they are sensitized to. Bet v 1 has been associated with Mal d 1 (apple), and Pru p 4 (peach) has been associated with Bet v 2.<sup>51</sup>

Art v 3 (mugwort) is an LTP that has been shown to cross-react to Pru p 3 (peach) as well as Cas s 8 (chestnut).<sup>61</sup> Ragweed has been associated with banana, melons, kiwi, and peaches.<sup>62</sup> Grasses have been associated with tomato, peach, and apple.<sup>29,63,64</sup>

**Table 4**

A compilation of PR-10 components for foods and aeroallergens

| PR-10        |         |            |                      |
|--------------|---------|------------|----------------------|
| Aeroallergen | Foods   |            |                      |
| Alder        | Aln g 1 | Apple      | Mal d 1              |
| Beech        | Fag s 1 | Apricot    | Pru ar 1             |
| Birch        | Bet v 1 | Carrot     | Dau c 1              |
| Hornbeam     | Car b 1 | Celery     | Api g 1              |
| White Oak    | Que a 1 | Cherry     | Pru av 1             |
|              |         | Chestnut   | Cas s 1              |
|              |         | Hazelnut   | Cor a 1              |
|              |         | Kiwi       | Act c 8, Act d 8, 11 |
|              |         | Mungbean   | Vig r 1              |
|              |         | Peanut     | Ara h 8              |
|              |         | Pear       | Pyr c 1              |
|              |         | Raspberry  | Rub i 1              |
|              |         | Soybean    | Gly m 4              |
|              |         | Strawberry | Fra a 1              |
|              |         | Tomato     | Sola l 4             |
|              |         | Walnut     | Jug r 5              |

**Table 5**

A compilation of profilin components for foods and aeroallergens

| Profilin family          |          |                   |          |
|--------------------------|----------|-------------------|----------|
| Aeroallergen             |          | Foods             |          |
| Bermuda grass            | Cyn d 12 | Almond            | Pru du 4 |
| Birch                    | Bet v 2  | Apple             | Mal d 4  |
| Burning bush             | Koc s 2  | Banana            | Mus a 1  |
| Date palm                | Pho d 2  | Barley            | Hor v 12 |
| Lambsquarter             | Che a 2  | Carrot            | Dau c 4  |
| Mesquite                 | Pro j 2  | Celery            | Api g 4  |
| Mugwort                  | Art v 4  | Cherry            | Pru av 4 |
| Para rubber tree (latex) | Hev b 8  | Chili/bell pepper | Cap a 2  |
| Pellitory-of-the-wall    | Par j 3  | Hazelnut          | Cor a 2  |
| Needle brush             | Aca f 2  | Kiwi              | Act d 9  |
| Pigweed                  | Ama r 2  | Lupine            | Lup a 5  |
| Ragweed                  | Amb a 8  | Lychee            | Lit c 1  |
| Russian thistle          | Sal k 4  | Muskmelon         | Cuc m 2  |
| Storage mite             | Tyr p 36 | Olive             | Ole e 2  |
| Timothy grass            | Phl p 12 | Orange            | Cit s 2  |
|                          |          | Peach             | Pru p 4  |
|                          |          | Peanut            | Ara h 5  |
|                          |          | Pear              | Pyr c 4  |
|                          |          | Pineapple         | Ana c 1  |
|                          |          | Rice              | Ory s 12 |
|                          |          | Soybean           | Gly m 3  |
|                          |          | Strawberry        | Fra a 4  |
|                          |          | Sunflower         | Hel a 2  |
|                          |          | Tomato            | Sola l 1 |
|                          |          | Walnut            | Jug r 7  |
|                          |          | Watermelon        | Citr l 2 |
|                          |          | Wheat             | Tri a 12 |
|                          |          | Yellow mustard    | Sin a 4  |

## Treatment

With all of the various definitions of food allergy as well as varying opinions of what constitutes PFAS, treatment for this condition varies widely. A study of US allergists in 2003 by Ma et al<sup>25</sup> showed that patients with class 1 food allergy are frequently diagnosed with PFAS.<sup>25</sup> This could lead to suboptimal care of potentially life-threatening food allergies. However, that would depend on how those allergists treat PFAS.

In a study in the United Kingdom, 18% of allergists had never recommended an epinephrine auto injector (EAI) for treatment of PFAS, compared with 70% of allergists in the United States who

**Table 6**

Common clinically relevant PFAS allergens

| Relevant PFAS allergens |                          |
|-------------------------|--------------------------|
| Primary sensitization   | Cross-reactive allergens |
| Profilin examples:      | Kiwi (Act d 9)           |
| Birch                   | Pineapple (Ana c 1)      |
| Mugwort                 | Celery (Api g 4)         |
| Ragweed                 | Peanut (Ara h 5)         |
|                         | Carrot (Dau c 4)         |
|                         | Soy (Gly m 3)            |
|                         | Apple (Mal d 4)          |
|                         | Banana (Mus a 1)         |
|                         | Peach (Pru p 4)          |
| PR-10 proteins examples | Peach (Pru p 1)          |
| Birch (Bet v 1)         | Apple (Mal d 1)          |
| Oak (Que a 1)           | Peanut (Ara h 8)         |
|                         | Hazelnut (Cor a 1)       |
|                         | Soy (Gly m 4)            |
|                         | Celery (Api g 1)         |
| LTP examples            | Kiwi (Act d 10)          |
| Ragweed (Amb a 6)       | Peanut (Ara h 9)         |
| Mugwort (Art v 3)       | Hazelnut (Cor a 8)       |
|                         | Latex (Hev b 12)         |
|                         | Walnut (Jug r 3)         |
|                         | Apple (Mal d 3)          |
|                         | Wheat (Tri a 14)         |
|                         | Peach (Pru p 3)          |

claimed they would consider an EAI for PFAS.<sup>25,65</sup> In this study, the reasons cited by US allergists for needing an EAI were a reaction that involved lower airway symptoms (89%), current diagnosis of asthma (39%), pharyngeal symptoms (58%), facial angioedema (31%), and generalized urticaria (19%).

The 2014 update to the food allergy practice parameters states, "Patients with a history of laryngeal swelling or respiratory compromise should avoid raw foods strictly and be prescribed an epinephrine auto injector."<sup>66</sup> Although this does not encompass all of the reasons cited by the physicians for prescribing an EAI, it does show that in the event of a history of severe reaction, prescription of an EAI is reasonable.

Depending on the food components patients are sensitized to, risk varies for the component to remain stable through digestion. Because of this stability, the allergen's antigenic properties have the potential to be maintained. As mentioned previously, LTPs have been shown to be highly cross-reactive, suggesting a potential benefit to avoidance of additional foods.<sup>47</sup> Two methods for obtaining components are ImmunoCAP ISAC and AllergyExplorer (ALEX). These test numerous allergens, with amounts of 112 components and 125 components, respectively. Panels of components have been used in the past to help diagnose PFAS.<sup>67</sup> The utility of getting testing performed on proteins to which the patient has not been experiencing clinical symptoms has been questioned. In practicality, however, individually ordering components for all of the allergens the provider may be concerned about may not be feasible, and a larger panel may help streamline the process. Ordering single IgE tests can be expensive, and to be cost effective ISAC would have to replace at least 13 single IgE tests.<sup>68</sup> By using these principles and knowledge of the pathogenesis of food allergens, one can have an individualized discussion with patients to ensure that they have their symptoms appropriately managed. One algorithm representing this discussion is shown in Figure 1.

One survey by Ma et al<sup>25</sup> showed that 30% of providers never prescribed EIA for PFAS, and 20% of providers diagnosed a systemic reaction to peach as OAS.<sup>25</sup> Although avoidance measures of class I allergens are commonly recommended, food avoidance does not seem to have any lasting treatment benefit in class II allergens. Perhaps this phenomenon is attributable to continued exposure to the original sensitizing agent.<sup>69–71</sup> In fact, reports have been made of patients developing tolerance to foods such as carrots and apples, thought to be continued exposure with oral immunotherapy.<sup>72,73</sup>

Apart from avoidance, education, or EAI, given that the primary sensitizer in class II allergens is typically a pollen, both subcutaneous immunotherapy (SCIT) and sublingual immunotherapy (SLIT) have been studied to see whether tolerance to provocative foods can be increased. One study enrolled 74 birch-allergic patients in a double blinded placebo-controlled trial in a comparison between SLIT and SCIT.<sup>74</sup> In that study, no significant difference was noted between SLIT, SCIT, or placebo when comparing pre-treatment oral food challenges (OFC) with post-treatment OFCs. Another study by Asero<sup>75</sup> looked prospectively at 49 birch-sensitive patients with positive PFAS to apple, who had received SCIT for 1 to 3 years.<sup>75</sup> In that study, 80% of patients reported subjective improvement in their symptoms to apples; of those, 54% showed complete resolution of their symptoms. Immunotherapy, however, is not without its risks, as SLIT improved apple allergy in 1 of 11 patients but induced apple allergy in 3 of 11 patients in the study by Hansen et al.<sup>74</sup>

Overall, the literature regarding the benefits of SLIT/SCIT to PFAS conflicts with some studies showing potential benefits, whereas others show none. Most of the research available are patients with apple allergy being treated with birch pollen.<sup>75–81</sup> Newer biologics are now available that have been shown to help in many atopic conditions. One that has been looked at for PFAS is omalizumab. An observational study of 46 patients on omalizumab or SCIT showed

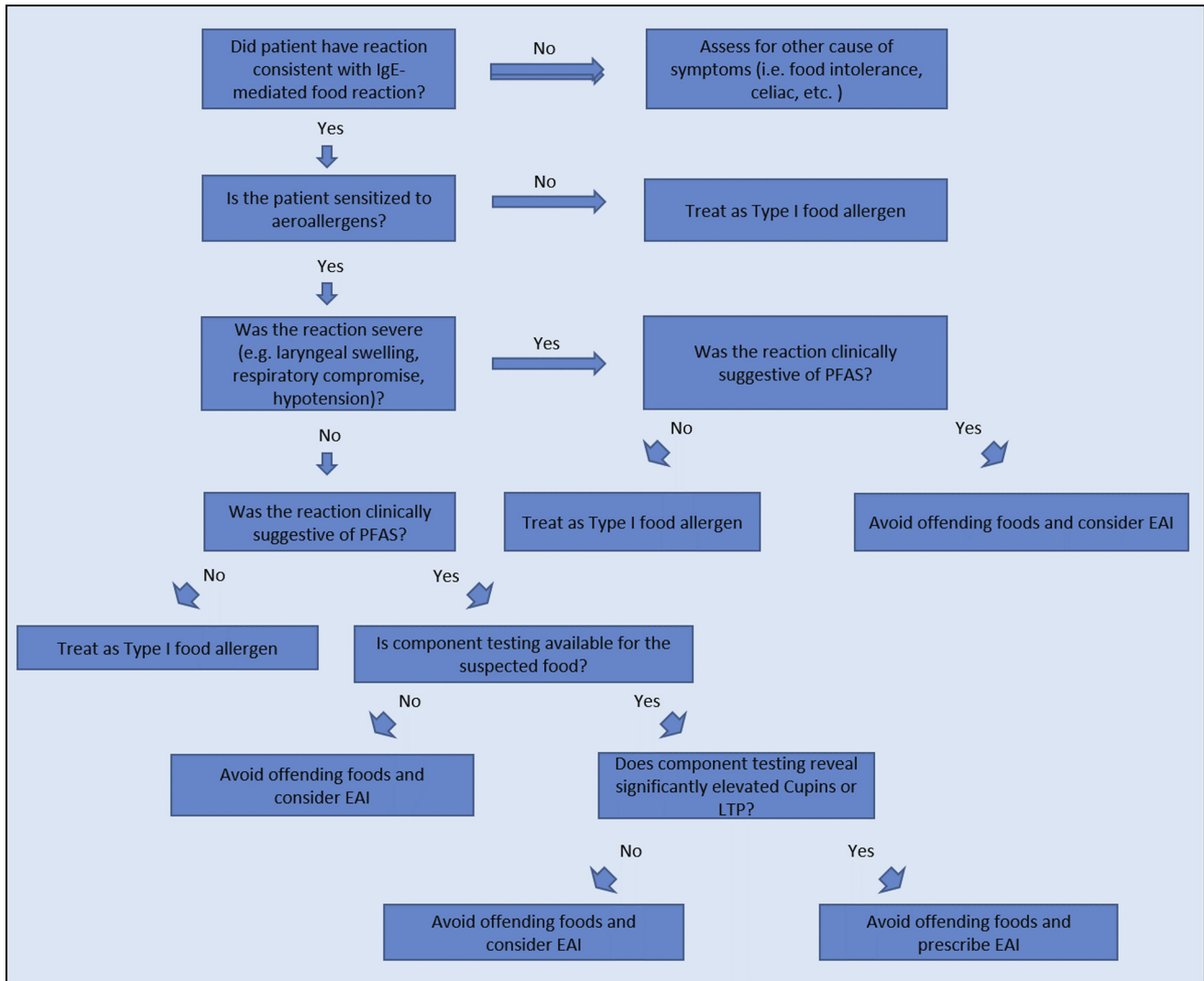


**Figure 1.** Algorithm for the approach to PFAS.

no statistical difference in symptoms in patients among those receiving omalizumab alone, omalizumab with SCIT, or SCIT alone.<sup>82</sup> Some concern has been raised about the potential allergenicity of genetically modified (GM) foods. A systematic review by Dunn et al<sup>83</sup> in 2017 concluded that “GM products do not appear to be more allergenic than their conventional counterpart as determined by IgE binding studies.” They went on to say that no data exist showing consumption of GM proteins causing allergy to develop in individuals who are not allergic at baseline.<sup>83</sup> The contrary may be true in that GM foods could have culprit proteins silenced, reducing their allergenicity, as reported by Dubois et al.<sup>84</sup>

## Conclusion

Pollen food allergy syndrome is caused primarily by class II allergens. This syndrome often results in several food allergies because of the homology between the plant proteins. The true prevalence of PFAS has yet to be defined, because it appears to be extremely variable based on geographical distribution. It has been shown, however, that it is a fairly prevalent condition, especially in the subset of atopic individuals. Because atopic individuals are the largest group of individuals evaluated by allergists, it behooves us to recognize the common presentations of early GI tract symptoms as well as the less common but more serious presentation of

systemic reactions and even anaphylactic shock. By early recognition and understanding of pathogenesis of PFAS, the provider can have a tailored discussion with the patient, which can include risks of reaction, severity of reaction, and potentially cross-reactive foods. Although an EAI is appropriate in high-risk reactions, it may not be suitable for all situations. Multiple factors affect this decision, to include difficulty in following strict diet restriction, quality of life, cost of EAI, and acceptable risk level to the patient and provider. As additional component testing becomes commercially available, knowledge of this subject will help ensure optimal medical management.

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