



Anaphylaxis across Europe: are pollen food syndrome and lipid transfer protein allergy so far apart?

Bianca Olivieri^a, Kostadin V. Stoenchev^b and Isabel J. Skypala^b

Purpose of review

Traditionally pollen-food syndrome (PFS) is considered to be a mild cross-reacting food allergy affecting only Northern Europe, with lipid transfer protein (LTP) allergy being more severe and mainly occurring in Southern Europe. This review seeks to update the reader on both types of plant food allergy and to determine whether the stereotypical presentations of these plant food allergies remain the same, with a particular focus on reaction severity.

Recent findings

Recent findings suggest that both these types of plant food allergy occur in children and adults. Although it is true that PFS allergy is more prevalent in Northern Europe and LTP allergy is more well known in Southern Europe, these conditions are not hidebound by geography, and the increasing spread and allergenicity of pollen due to global warming continues to change their presentation. Both conditions have a spectrum of symptom severity, with PFS sometimes presenting with more severe symptoms, including anaphylaxis and LTP allergy with milder reactions.

Summary

It is important to consider that in many parts of Europe, reactions to plant foods, especially fruits or vegetables, could be mediated either by pollen cross-reactivity or primary sensitization to LTP allergens. All those presenting with symptoms to plant foods will benefit from a detailed clinical history and appropriate tests so that an accurate diagnosis can be made, and correct management implemented.

Keywords

anaphylaxis, food allergy, lipid transfer protein, pollen, pollen-food syndrome

INTRODUCTION

Food allergy in Europe is widespread but the prevalence and foods involved vary. Plant food pan allergens are highly relevant triggers in both children and adults, although there are strong geographical differences likely due to primary sensitization either to specific pollens (birch, grass, mugwort or ragweed) or to nonspecific lipid transfer proteins (LTPs) [1,2]. Reactions to multiple foods are commonly reported in those sensitized to LTP, often Pru p 3 from peaches, due to cross-reactions with LTP in often botanically unrelated fruits, vegetables, legumes and nuts [3,4]. Pollen-food syndrome (PFS) occurs when cross-reactivity occurs either between the pathogenesis-related 10 (PR10) proteins and the major birch allergen Bet v 1, or between profilins in foods and those in tree, grass or weed pollens [5]. Although often involving similar foods, these common plant food allergies are

considered to have different presenting features, especially with regard to symptom severity, age of onset and geographical location. This review highlights the key similarities and differences between PFS and LTP allergy, with regard to age, geography, symptom severity, foods involved and cofactors.

^aDepartment of Medicine, Asthma, Allergy and Clinical Immunology Section, University of Verona, Verona, Italy and ^bRoyal Brompton & Harefield Hospitals, Part of Guys and St Thomas NHS Foundation Trust, London, United Kingdom

Correspondence to Isabel J. Skypala, Department of Allergy & Clinical Immunology, Royal Brompton Hospital, Sydney Street, London SW3 6NP, United Kingdom. Tel: +44 0330 128 8992; fax: +44 0330 128 7780; e-mail: i.skypala@rbht.nhs.uk

Curr Opin Allergy Clin Immunol 2022, 22:291–297

DOI:10.1097/ACI.0000000000000847

KEY POINTS

- PFS can manifest with severe or anaphylactic symptoms.
- The spread and increasing levels of pollens influence the prevalence of PFS and type of foods involved.
- LTP allergy is present in both Southern and Northern Europe but it is still not clear what the role is of LTP allergens in pollens, and whether they can be primary sensitizing allergens.
- Some foods might still trigger PFS when cooked, and LTP allergens from tomato, onion or garlic could be present in composite foods such as pizza and ready-meals.
- Cofactors are particularly relevant in LTP allergy, and the suppression of gastric acid through the use of proton pump inhibitors, or undertaking bariatric surgery could lead to individuals with PFS experiencing more severe reactions.

EPIDEMIOLOGY

Although there have been several publications evaluating the prevalence of PFS and LTP allergy in different age groups, other factors such as ethnicity, sex and social determinants have been less well studied.

AGE

Both PFS and LTP allergy occur across a wide age spectrum. PFS is rarely described in infancy because its cause is related to pollen sensitization. A review by Mastrorilli *et al.* [6] found that the prevalence of PFS in children ranged from 5 to 48%, and risk factors for PFS were female sex, older age, parents affected by atopic diseases, being overweight and environmental tobacco smoke exposure. Kim *et al.* [7] reported a high prevalence of PFS in children with atopic dermatitis and birch sensitization, with high birch specific-IgE levels linked to an increased likelihood of having PFS. The prevalence of PFS is higher in birch-endemic areas in Northern Europe; only 3.3% of 672 pollen-sensitized Spanish children had PFS-related symptoms [8]. LTP allergy, commonly described in adults, is also an emerging allergen in the paediatric population. Not much is yet known about this type of allergy in children so it often remains underdiagnosed [9]. In 82 children with allergic rhinitis due to *Parietaria* pollen and sensitization to Pru p 3, about one-quarter reported anaphylaxis after eating LTP-containing foods, about half

reported oral allergy symptoms (OAS) and one-quarter were only sensitized to Pru p 3 but asymptomatic [10]. In another study of 26 children with positive skin prick test (SPT) to peach extract and sIgE to Pru p 3, the symptoms described were urticaria in 58%, anaphylaxis in 46% and OAS in 42%. There was no association between the incidence of severe reactions and levels of sIgE to Pru p 3 or Cor a 8, or with SPT wheal size. Furthermore, 69% of patients had multiple reactions with more than one food, and cofactors were reported in 27% and associated with more severe reactions. In some children, cofactors were essential for the occurrence of reactions and were associated with anaphylaxis, as in adults [11].

SEX, RACE AND SOCIAL DETERMINANTS

There are fewer data concerning other epidemiological factors such as ethnicity, social determinants and sex on either the prevalence or severity of PFS or LTP allergy. One significant finding from a large study of PFS in seven Southern European countries was that 7.8% of individuals with PFS had a mother who also had PFS compared with 1.9% of controls [12]. It is known that sex differences may influence food allergy symptoms, as well as immune reactivity, which vary during menstrual cycle, pregnancy, hormone replacement therapy and menopause possibly due to changes in oestrogen and progesterone levels promoting a Th2 polarization [13]. A study of 6824 adults that PFS significantly affected more than twice as many women as men (13.1 vs. 5.7% of the whole cohort); also men developed PFS earlier in life (teens to 30s), whereas women were older when they developed PFS and continued to develop PFS into their 60s [14]. Another study of pollen-sensitized patients with a mean age of 12 years, found that being female was a potential risk factor for the development of PFS [8]. There is less evidence for sex differences in LTP allergy, but in a large follow-up study, during a period of 10 years, patients sensitized to LTP experienced symptoms of allergy to previously tolerated plant foods, with a higher prevalence of female patients (60%) [15^{***}]. Another study found that women were more likely to have cofactor-dependent LTP allergy, possibly linked to menstruation [16]. There is very little evidence to determine whether social determinants or ethnicity are relevant factors in the prevalence of PFS or LTP allergy. A workgroup report from the American Academy of Asthma, Allergy & Clinical Immunology concluded those in minority ethnic groups, or who had low incomes or lived in a rural area had increased food allergic disease [17].

SYMPTOM TYPE AND SEVERITY

The usual symptoms of PFS are rapid-onset mild pruritis and angioedema affecting the oral cavity. Other more troublesome symptoms can occur, including paraesthesia of the lip or tongue, difficulty swallowing, ear itching, rhino-conjunctivitis, nausea and sometimes laryngeal tightness but more severe or anaphylactic episodes are considered to be rare [18]. Those diagnosed with LTP allergy can present with an extremely wide and varied spectrum of symptoms which include contact urticaria, oropharyngeal symptoms, angioedema, respiratory symptoms, gastrointestinal symptoms and anaphylaxis [19[¶]].

ANAPHYLAXIS

Reactions involving stable proteins such as LTP are associated with a higher risk of severe reactions, unlike the labile allergens involved in PFS. However, recent studies suggest that as many as 10% of individuals with PFS may experience systemic or anaphylactic reactions [20,21]. A number of factors could affect the symptom type and severity of both PFS and LTP allergy, including the number of sensitizing allergens, the level of sensitization, cosensitization, the number of food triggers reported, presence of cofactors and stability of the allergenic proteins – see Fig. 1. Thus, it is important to ensure that all those with either PFS or LTP allergy are individually assessed for the risk of an anaphylactic reaction, and consequent need to carry epinephrine, based on their clinical history. A review of their sensitization to foods and aeroallergens can also provide clues as to the likelihood of a severe reactions.

SENSITIZATION PATTERNS AND SYMPTOM SEVERITY

Polysensitization may affect symptom type and severity in individuals with PFS; Högerle *et al.* [22] reported that in a cohort of 1119 patients, those with PFS who were sensitized to both Bet v 1 and a profilin were more likely to report oral itching, swelling and gastrointestinal discomfort, experience more severe rhinitis and a higher tendency to develop asthma than those sensitized to Bet v 1 alone. The number of PFS food triggers may also be linked to symptom severity; Kim *et al.* [20] reported that individuals with PFS who experienced reported anaphylaxis had a significantly higher number of causative food triggers and had a greater strength of sensitization to trees, timothy grass and ragweed. The same phenomenon can occur with LTP allergy. Individuals who are sensitized and

reactive to LTP in multiple foods are considered to have LTP syndrome, and reactions to five or more triggers are associated with increased symptom severity [19[¶]]. This finding has been confirmed by Ruano-Zaragoza *et al.* in a study of over 400 individuals with LTP allergy, 37% of whom had experienced anaphylaxis, which was especially prevalent in those sensitized to five or more LTPs. However, symptom severity varied with urticaria and oral allergy syndrome being common, suggesting that sensitization to LTP allergens does not always correspond to severe reactions [16].

It is possible that there is an association between the level of sensitization and systemic or severe reactions; a review of LTP allergy by Asero *et al.* [23], highlighted evidence that those experiencing systemic reactions to foods were more likely to have a higher level of specific IgE to LTP. Scheurer *et al.* [24^{¶¶}] reported that mono-sensitization to LTP allergens was much more frequent in the Mediterranean basin and is associated with more severe reactions compared with individuals from Central and Northern Europe who are often cosensitized to birch and other pollens. A recent study from Bogas *et al.* [25] found concomitant sensitization to LTP and profilins appeared to be protective against severe reactions, and could be a useful biomarker of severity rather than the number of LTP sensitizations. There is not currently much evidence on the severity of LTP allergy in Northern Europe, but Decuyper *et al.* [26] recently compared LTP-sensitized individuals from Spain and Belgium and found that symptomatic patients from Spain were more sensitive to lower allergen concentrations compared with those from Belgium.

COFACTORS AND SYMPTOM SEVERITY

Cofactor presence is also generally associated with increased reaction severity. The best characterized cofactors include exercise, NSAIDs and alcohol, though numerous others have been proposed (e.g. sleep deprivation and concurrent viral infection). The hypothesized mechanisms of action were recently reviewed by Muñoz-Cano *et al.* [27] and include an increase in gut permeability, changes in plasma osmolarity, blood flow redistribution, basophil and mast cell activity, diamine oxidase inhibition and metabolism of eicosanoids and adenosine. Cofactor involvement in LTP allergy has been described in numerous studies to date. A recent prospective multicentre study showed that of 52 patients with food-dependent NSAID-induced hypersensitivity, 44 (85%) were due to LTP, 75% of which were sensitized to three or more LTP foods [28]. LTP accounted for 85% of anaphylaxis cases.

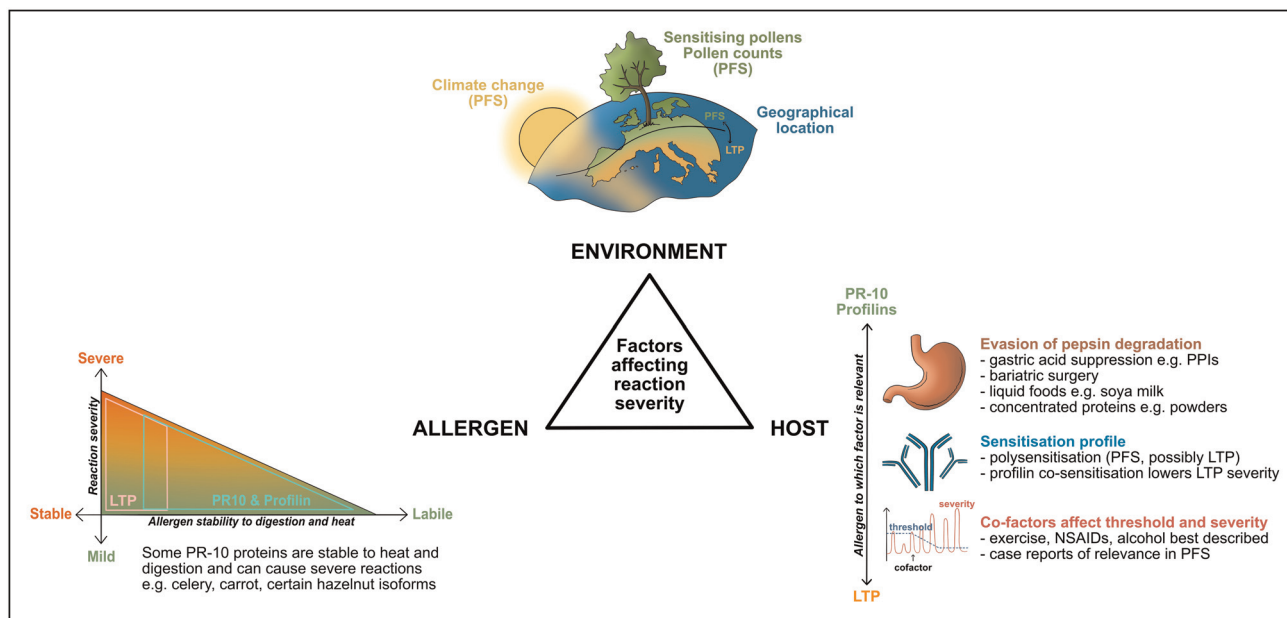


FIGURE 1. Factors affecting reaction severity in pollen-food syndrome and lipid transfer protein allergy: host, environment and allergen-related factors.

Furthermore, most patients tolerated the culprit foods in the absence of NSAIDs and the rest experienced mild symptoms only. There is little data with regards to alcohol, though a recent retrospective study of 157 LTP allergic patients reported alcohol as the cofactor in 10% of cases, following exercise (32%) and NSAIDs (16%). It is also important not to overlook alcohol as the source of LTP (e.g. cereal grains in beer) in addition to its cofactor effect [29]. Although PFS is generally not cofactor dependent, case reports of systemic reactions to PR-10 proteins in the context of cofactors are emerging [21,30].

FOOD TRIGGERS, DIGESTION AND SYMPTOM SEVERITY

Foods triggering symptoms in individuals with either PFS or LTP allergy are often very similar, but the point of difference between these two plant food allergies is that PR10 and profilin allergens are heat labile and easily degraded by gastric acid, so processed or cooked versions of foods are usually tolerated [5]. However, LTPs are present in both raw, cooked and processed foods, as they are highly resistant to degradation by heat and digestion [3^o]. Processed foods such as pizza have been reported to trigger reactions in individuals sensitized to LTP, and a recent case report demonstrated that LTP allergens in tomato were one of the causes of significant reactions to pizza [31]. The wide distribution of LTP allergens in so many plant foods

might be another reason why individuals with LTP allergy react to composite foods. Onions and garlic, present in many ready-prepared and restaurant meals, have recently been demonstrated to be the cause of food allergic reactions in 27 of 924 patients, and likely caused by LTP allergens [32^o].

Gastric acid promotes the conversion of inactive pepsinogen to active pepsin, but acid suppression with protein pump inhibitors (PPIs), antacids and H2 receptor antagonists reduces pepsin levels and thus affect the digestion of PR-10 and profilin allergens. Pepsin's protective effect was demonstrated by a recent retrospective multicentre study by Asero *et al.* [23] which showed a significantly higher prevalence of PPI use among PFS patients with a history of systemic reactions compared with controls matched for age, sex and sensitization profile who experienced local symptoms only. Liquid foods transiently increase gastric pH and pass through the stomach more rapidly than solid foods and plant food drinks such as smoothies, milkshakes also have higher concentrations of PR-10 and profilin proteins. These factors contribute to the ability to evade pepsin's protection. Asero *et al.* [23] also demonstrated that soya milk has a significantly higher propensity to provoke systemic rather than local reactions in Gly m 4 allergic patients.

Similarly, bariatric surgery such as Roux-en-Y gastric bypass and sleeve gastrectomy reduce numbers of pepsin-secreting Chief cells and result in significant reduction in pepsinogen levels [33]. Case reports have described worsening of PFS reaction

severity post bariatric surgery [34]. Given the correct circumstances, labile plant proteins can therefore cause systemic reactions akin to nsLTP allergy. Further similarities to nsLTP arise when considering the stability of certain PR-10 proteins to heat and acidity. A recent study by Fühner *et al.* [35] examined four isoforms of Hazelnut's PR-10 protein Cor a 1 and found that despite their highly similar sequences and three-dimensional structures, the isoforms exhibit significant differences in structural flexibility, heat resistance and specific IgE binding. A similar observation was reported for the PR-10 protein of carrot, Dau c 1, most of the isoforms of which can refold at physiological pH and so it remains allergenic despite cooking [36].

EFFECT OF POLLEN SENSITISATION, CLIMATE CHANGE AND POLLUTION ON SYMPTOM SEVERITY

Those with PFS are more likely to react, or have more severe reactions, during the pollen season. Gabrielli *et al.* [37] recruited and reviewed 250 patients with fruit-induced anaphylaxis, and reported that severe reactions to fruit were more likely to occur in spring, proposing pollen cross-reactivity as the cause. In Northern Europe PFS is highly prevalent and principally mediated by Bet v 1, the major pollen allergen in *Betula verrucosa* (Silver birch), although individuals sensitized and allergic to oak pollen can also be symptomatic on exposure to birch pollen and thus may also experience PFS [5,38]. The birch profilin Bet v 2 can also mediate PFS reactions in up to 20% of Northern European populations, but is a more common sensitizing allergen in Central and Southern Europe [5]. A recent study by Lipp *et al.* [12] demonstrated that 20% of patients with seasonal allergic rhinitis from Southern European countries had PFS, kiwi, peach and melon most likely to elicit reactions. Profilins from grass (*Phleum pratense*) Phl p 12, mugwort (*Artemisia vulgaris*) Art v 4, or ragweed (*Ambrosia artemisiifolia*) Amb a 8, are also important mediators of PFS in these populations and their abundance in plants means reactions are often triggered by multiple foods [39]. Several studies have demonstrated an increase in sensitization to birch tree pollen, but other pollens are also becoming more widespread and increasingly more allergenic. The spread of ragweed is increasing in Northern and Eastern European countries, probably due to climate change [40]. Sensitization rates to ragweed increased in Germany by nearly 70% over 2 decades, alongside continuing high levels of cosensitization to birch and grass pollen [41]. In Basel, Switzerland, temperature increases over the last 50 years have correlated with an earlier start date

and increased intensity of the tree pollen season [42]. A study using time-series regression models reported that an increase in the peak concentrations of tree and weed pollens between 2002 and 2019 was significantly associated with temperature and precipitation [43]. Such changes may also increase the incidence and severity of PFS. In a study of two random cohorts 20 years apart, Loraud *et al.* reported a highly significant increase in sensitization to trees, allergic rhinitis and PFS in children aged 7–15 years who were under the asthma team [44[¶]].

CAN POLLEN ACT AS A PRIMARY SENSITIZER OF LIPID TRANSFER PROTEIN ALLERGY?

Sensitization and symptoms provoked by LTP allergens have traditionally occurred mainly in Southern Europe, but individuals in Northern European countries, including Belgium, Austria, United Kingdom and more recently Poland, are also sensitized and symptomatic to LTP [3[¶],45]. Could this increase be linked to pollens and could pollen LTPs act as the primary sensitizer in individuals who also react to LTP in foods? An excellent review by Scheurer *et al.* [24^{¶¶}] found that there was conflicting evidence from Southern Europe as to whether sensitization to pollen LTP such as from plane tree (Pla a 3) and Mugwort (Art v 3) could be linked to sensitization to food. Although previous studies have suggested primary sensitization to Art v 1 was linked with symptoms to peach, in some populations, sensitization to the mugwort pollen LTP Art v 3 seems to indicate season-specific pollen-related food allergy rather than LTP allergy [46]. Asero *et al.* [47] reported that although sensitization to Art v 3 and Pla a 3 was common in their Pru p 3-sensitized population, Pru p 3 IgE reactivity was not inhibited by mugwort or plane tree pollen extracts so evidence for them being primary LTP sensitizers is lacking. There is less evidence for the role of the Plane tree LTP Pla a 3 being a primary sensitizing allergen, even in areas such as Madrid, which has high levels of LTP allergy and the highest concentration of plane tree pollen in Spain, but sensitization is usually to Pla a 2, rather than Pla a 3 [48]. However, a recent review described how plane trees produce large amounts of pollen during the springtime which could contain much higher levels of the allergens Pla a 1 and Pla a 3 in areas with high levels of pollutant gases and vehicle exhaust particles [49]. So, could pollution and city planning be the reason for the development of LTP allergy in Northern Europe? A recent review of current controversies of LTP allergy suggested that primary sensitization could be to peach, to pollen (Pla a 3, Art v 3) or even to the cannabis LTP Can s 3 [50[¶]].

CONCLUSION

The diagnosis and management of PFS and LTP allergy needs careful consideration and long-term follow-up. An excellent review of allergy to foods from the Rosaceae family by Costa and Mafra highlighted the major differences between diverse plant food allergies, and emphasized the importance of individualized advice and risk stratification [51[■]]. There are still questions over the avoidance of high risk foods, especially as it has been demonstrated that almost one third of individuals with plant food allergy, and sensitized to LTP, experienced reactions to previously tolerated fruits and nuts 10 years after diagnosis [15[■]]. It is currently unknown whether those with PFS will inevitably react to more foods over time, and if so whether this is due to changes in their pollen sensitization profile. Plant food allergy is changing. Reactions to individual plant food suggest a primary allergy to a seed storage protein. When multiple plant foods trigger symptoms, including nuts, fruits and vegetables, then a diagnosis of PFS or LTP allergy should be considered, whatever the status of the patient is with regards to their age, geographical location, symptom severity or pollen sensitization.

Acknowledgements

None.

Financial support and sponsorship

B.O. is the recipient of an EAACI Clinical Fellowship 2022.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Lyons SA, Clausen M, Knulst AC, *et al.* Prevalence of food sensitization and food allergy in children across Europe. *J Allergy Clin Immunol Pract* 2020; 8:2736–2746.e2739.
 2. Lyons SA, Burney PGJ, Ballmer-Weber BK, *et al.* Food allergy in adults: substantial variation in prevalence and causative foods across Europe. *J Allergy Clin Immunol Pract* 2019; 7:1920–1928.e1911.
 3. Skypala IJ, Asero R, Barber D, *et al.* Nonspecific lipid-transfer proteins: ■ allergen structure and function, cross-reactivity, sensitization, and epidemiology. *Clin Transl Allergy* 2021; 11:e12010.
- This is a wide ranging review of the subject of lipid transfer protein allergens.
4. Yagami A, Ebisawa M. New findings, pathophysiology, and antigen analysis in pollen-food allergy syndrome. *Curr Opin Allergy Clin Immunol* 2019; 19:218–223.
 5. Skypala IJ, Krishna HH, Rey-Garcia MT, *et al.* BSACI guideline for the diagnosis and management of pollen food syndrome in the UK. *Clin Exp Allergy* 2022; In press.
 6. Mastrorilli C, Cardinale F, Giannetti A, Caffarelli C. Pollen-food allergy syndrome: a not so rare disease in childhood. *Medicina (Kaunas)* 2019; 55:641.

7. Kim KI, Lee B, Min TK, *et al.* Clinical characteristics of oral allergy syndrome in children with atopic dermatitis and birch sensitization: a single center study. *J Korean Med Sci* 2019; 34:e11.
 8. Guvenir H, Dibek Misirliglu E, Buyuktiryaki B, *et al.* Frequency and clinical features of pollen-food syndrome in children. *Allergol Immunopathol (Madr)* 2020; 48:78–83.
 9. Aruanno A, Urbani S, Frati F, Nucera E. LTP allergy/sensitization in a pediatric population. *Allergol Immunopathol (Madr)* 2020; 48:763–770.
 10. Ciprandi G, Del Barba P, Silvestri M, *et al.* Pru p 3 sensitization in children with allergy to *Parietaria pollens*. *Acta Biomed* 2019; 90:265–268.
 11. Barradas Lopes J, Santa C, Valente C, *et al.* Allergy to lipid transfer proteins (LTP) in a pediatric population. *Eur Ann Allergy Clin Immunol* 2021. [Online ahead of print]
 12. Lipp T, Acar ahin A, Aggelidis X, *et al.* Heterogeneity of pollen food allergy syndrome in seven Southern European countries: the @IT.2020 multicenter study. *Allergy* 2021; 76:3041–3052.
 13. Pali-Schöll I, Jensen-Jarolim E. Gender aspects in food allergy. *Curr Opin Allergy Clin Immunol* 2019; 19:249–255.
 14. Osawa Y, Ito Y, Takahashi N, *et al.* Epidemiological study of oral allergy syndrome in birch pollen dispersal-free regions. *Allergol Int* 2020; 69:246–252.
 15. Betancor D, Gomez-Lopez A, Villalobos-Vilda C, *et al.* LTP allergy follow-up ■ study: development of allergy to new plant foods 10 years later. *Nutrients* 2021; 13:2165.
- Really important study which needs to be replicated for pollen-food syndrome (PFS).
16. Ruano-Zaragoza M, Somoza ML, Jiménez-Rodríguez TW, *et al.* Lipid transfer protein sensitization: risk of anaphylaxis and molecular sensitization profile in Pru p 3-sensitized patients. *Int Arch Allergy Immunol* 2021; 182:425–432.
 17. Davis CM, Apter AJ, Casillas A, *et al.* Health disparities in allergic and immunologic conditions in racial and ethnic underserved populations: a work group report of the AAAAI Committee on the Underserved. *J Allergy Clin Immunol* 2021; 147:1579–1593.
 18. Carlson G, Coop C. Pollen food allergy syndrome (PFAS): A review of current available literature. *Ann Allergy Asthma Immunol* 2019; 123:359–365.
 19. Skypala IJ, Bartra J, Ebo DG, *et al.* The diagnosis and management of allergic ■ reactions in patients sensitized to nonspecific lipid transfer proteins. *Allergy* 2021; 76:2433–2446.
- A comprehensive review of the diagnosis and management of lipid transfer protein (LTP) allergy.
20. Kim M, Ahn Y, Yoo Y, *et al.* Clinical manifestations and risk factors of anaphylaxis in pollen-food allergy syndrome. *Yonsei Med J* 2019; 60:960–968.
 21. Skypala IJ. Can patients with oral allergy syndrome be at risk of anaphylaxis? *Curr Opin Allergy Clin Immunol* 2020; 20:459–464.
 22. Högerle C, San Nicolo M, Gellrich D, *et al.* Clinical relevance of profilin sensitization concerning oral allergy syndrome in birch pollen sensitized patients. *J Asthma Allergy* 2022; 15:249–255.
 23. Asero R, Ariano R, Aruanno A, *et al.* Systemic allergic reactions induced by labile plant-food allergens: seeking potential cofactors. A multicenter study. *Allergy* 2021; 76:1473–1479.
 24. Scheurer S, van Ree R, Vieths S. The role of lipid transfer proteins as food and ■ pollen allergens outside the Mediterranean area. *Curr Allergy Asthma Rep* 2021; 21:7.
- This is an excellent, comprehensive and well written review of LTPs which discusses the evidence for LTP allergy beyond the Mediterranean countries.
25. Bogas G, Muñoz-Cano R, Mayorga C, *et al.* Phenotyping peach-allergic patients sensitized to lipid transfer protein and analysing severity biomarkers. *Allergy* 2020; 75:3228–3236.
 26. Decuyper II, Pascal M, Van Gasse AL, *et al.* Performance of basophil activation test and specific IgG4 as diagnostic tools in nonspecific lipid transfer protein allergy: Antwerp-Barcelona comparison. *Allergy* 2020; 75:616–624.
 27. Muñoz-Cano R, San Bartolome C, Casas-Saucedo R, *et al.* Immune-mediated mechanisms in cofactor-dependent food allergy and anaphylaxis: effect of cofactors in basophils and mast cells. *Front Immunol* 2020; 11:623071.
 28. Sánchez-López J, Araujo G, Cardona V, *et al.* Food-dependent NSAID-induced hypersensitivity (FDNIH) reactions: unraveling the clinical features and risk factors. *Allergy* 2021; 76:1480–1492.
 29. Pita JS, Sousa N, Bartolome B, *et al.* Beer: an uncommon cause of anaphylaxis. *BMJ Case Rep* 2019; 12:e227723.
 30. Radlińska A, Gomółka K, Zaleska A, Mędrała W. Unusual clinical picture of food-dependent exercise-induced anaphylaxis associated with soybean allergy and a reverse sequence of causative factors. *Postepy Dermatol Alergol* 2021; 38:703–705.
 31. Martín-Pedraza L, Wangorsch A, Bueno-Díaz C, *et al.* 2S albumins and nsLTP are involved in anaphylaxis to pizza sauce: IgE recognition before and after allergen processing. *Food Chem* 2020; 321:126679.
 32. Armentia A, Martín-Armentia S, Pineda F, *et al.* Allergic hypersensitivity to ■ garlic and onion in children and adults. *Allergol Immunopathol (Madr)* 2020; 48:232–236.
- Onions and garlic are not often considered when determining the allergens responsible for reactions to composite foods. This study demonstrates the importance of considering all ingredients when trying to determine the likely trigger of food allergic reactions.

33. Han ML, Liou JM, Ser KH, *et al.* Changes of serum pepsinogen level and ABC classification after bariatric surgery. *J Formos Med Assoc* 2021; 120:1377–1385.
34. Kamau J, Kearny S, Jaworek A, *et al.* Anaphylactic food allergy after Roux-en-Y gastric bypass. *Cureus* 2021; 13:e17710.
35. Führer S, Kamenik AS, Zeindl R, *et al.* Inverse relation between structural flexibility and IgE reactivity of Cor a 1 hazelnut allergens. *Sci Rep* 2021; 11:4173.
36. Jacob T, Vogel L, Reuter A, *et al.* Food processing does not abolish the allergenicity of the carrot allergen Dau c 1: influence of pH, temperature, and the food matrix. *Mol Nutr Food Res* 2020; 64:e2000334.
37. Gabrielli S, Clarke AE, Morris J, *et al.* Fruit-induced anaphylaxis: clinical presentation and management. *J Allergy Clin Immunol Pract* 2021; 9:2825–2830.e2822.
38. Ramirez RM, Jacobs RL, Andrews CP. Birch-naïve, oak-allergic subjects' response to birch pollen in an environmental chamber. *Allergy Asthma Proc* 2022; 43:116–123.
39. Poncet P, Sénéchal H, Charpin D. Update on pollen-food allergy syndrome. *Expert Rev Clin Immunol* 2020; 16:561–578.
40. Röseler STM, Baron JM, Höflich C, *et al.* New inhalant plant allergens. *Allergol Select* 2020; 4:1–10.
41. Forkel S, Beutner C, Heetfeld A, *et al.* Allergic rhinitis to weed pollen in Germany: dominance by plantain, rising prevalence, and polysensitization rates over 20 years. *Int Arch Allergy Immunol* 2020; 181:128–135.
42. Gehrig R, Clot B. 50 Years of pollen monitoring in Basel (Switzerland) demonstrate the influence of climate change on airborne pollen. *Front Allergy* 2021; 2:677159.
43. Paudel B, Chu T, Chen M, *et al.* Increased duration of pollen and mold exposure are linked to climate change. *Sci Rep* 2021; 11:12816.
44. Loraud C, de Ménonville CT, Bourgoïn-Heck M, *et al.* Emergence of pollen ■ food allergy syndrome in asthmatic children in Paris. *Pediatr Allergy Immunol* 2021; 32:702–708.
Demonstrates the changes in prevalence of PFS.
45. Wawrzęńczyk A, Zbikowska-Gotz M, Wawrzęńczyk A, Bartuzi Z. Sensitisation to lipid transfer proteins in pollen – allergic adults with food allergy. *Postępy Dermatol Alergol* 2020; 37:508–512.
46. Li JD, Du ZR, Liu J, *et al.* Characteristics of pollen-related food allergy based on individual pollen allergy profiles in the Chinese population. *World Allergy Organ J* 2020; 13:100120.
47. Asero R, Brusca I, Cecchi L, *et al.* Why lipid transfer protein allergy is not a pollen-food syndrome: novel data and literature review. *Eur Ann Allergy Clin Immunol* 2021. [Online ahead of print]
48. Nuñez-Borque E, Betancor D, Fernández-Bravo S, *et al.* Allergen profile of London plane tree pollen: clinical and molecular pattern in central Spain. *J Investig Allergol Clin Immunol* 2021. [Online ahead of print]
49. Vranceanu D, Berghi ON, Cergan R, *et al.* Urban allergy review: allergic rhinitis and asthma with plane tree sensitization (Review). *Exp Ther Med* 2021; 21:275.
50. Asero R, Pravettoni V, Scala E, Villalta D. Lipid transfer protein allergy: a ■ review of current controversies. *Clin Exp Allergy* 2022; 52:222–230.
Brings the LTP story right up to date.
51. Costa J, Mafra I. Rosaceae food allergy: a review. *Crit Rev Food Sci Nutr* ■■ 2022; 3:1–38.
Very good comprehensive overview of the family that are common causes of symptoms in individuals with either PFS or LTP allergy.