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Anaphylaxis (M Sánchez-Borges, Section Editor)

Cereal Anaphylaxis

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Abstract

Purpose of review To summarize the current understanding and important aspects of anaphylaxis related to cereal grains.
Recent findings Skin applied products have recently shown to be associated with cereal anaphylaxis; advances in wheat antigen investigation are discussed; new evidence of cereal cross-reactivity; and oral immunotherapy has been attempted with some success.
Summary Cereal grains have been shown to cause anaphylaxis. Recent investigation into wheat antigens has led to identification of possible markers for WDEIA and wheat allergy. Cereal cross-reactivity has been noted, which is clinically relevant when treating cereal anaphylaxis.

Introduction

Cereal grains are found within the family Poaceae. Wheat, rice, oats, barley, corn, rye, sorghum, and millet are all part of this family and considered cereals. There are different varieties of wheat such as freekeh, farro, spelt, triticale (a mixture of wheat and rye), and emmer. In addition, there are pseudo-cereal grains, so named because they are not 'true' grains belonging to the Poaceae family, but are used in similar ways and nutritionally similar to the true grains. Pseudo cereals include amaranth, quinoa, and buckwheat [1].

Wheat

Of the cereal grains, wheat (*Triticum aestivum*) is the most common to cause food allergy. Wheat, along with peanut, egg, soy, and milk are responsible for about 90% of all food hypersensitivity reactions in children [2].

Wheat antigens

As with other foods, investigation into the specific antigens involved in wheat allergy has been undertaken. Important wheat allergens include α-amylase inhibitor (Tri a 28), ω-5 gliadin (Tri a 19), lipid transfer protein (Tri a 14), α-purothionin (Tri a 37), α/β-gliadin (Tri a 21), γ-gliadin (Tri a 20), and high-molecular weight (HMW) glutenin [3–10]. Table 1 lists various known wheat antigens, their nomenclature, and the association of the particular antigen with wheat-related disease. In broader terms, wheat proteins can be broken down into two groups: water-insoluble glutens and water-soluble proteins (e.g. α-amylase inhibitor) [7]. Gliadins belong to the former group and are classified depending on their electrophoretic mobility into α/β, γ, and ω-gliadins [7]. Sensitivity to different wheat antigens can help distinguish wheat allergy conditions. Tri a 37 sensitivity, for example, may be associated with increased risk of wheat-induced anaphylaxis [6]. ω-5 gliadin has been associated with wheat-dependent exercise-induced anaphylaxis (WDEIA) [4•, 8, 12].

One study found that about 80% of patients with WDEIA had IgE antibodies to ω-5 gliadin. The remainder of the patients had IgE to high-molecular weight glutenin (HMW-glutenin). It was proposed that evaluating for both of these antigens could be helpful in diagnosing WDEIA [12].

Finding specific IgE to both ω-5 gliadin and HMW-glutenin has also been proposed as a means to differentiate simple wheat/gluten sensitization versus WDEIA. One study looked at 30 WDEIA patients and 25 wheat/gluten sensitized patients, and showed that 29/30 of the WDEIA patients had specific IgE antibodies to ω-5 gliadin and HMW glutenin epitopes. 0/25 patients had both epitopes positive in the wheat/gluten-sensitized patients without WDEIA. Those in the wheat/gluten-sensitized group that did have a single antigen positive were weakly positive [4•].

α/β/γ-gliadins are other antigens that have been studied in wheat-related allergy. One study looked at 17 patients with WDEIA and found that 14/17 (82%) were positive for specific IgE to α/β/γ-gliadin, including 3 patients who

Table 1. Wheat antigens

Common name	Allergen nomenclature	Association
ω-5-gliadin	Tri a 19 [11]	WDEIA [4•, 8, 16]; wheat allergy presence [17]; persistent wheat allergy [13•, 18]
α-amylase inhibitor	Tri a 28 [12]	Baker's asthma [15]
Wheat lipid transfer protein	Tri a 14 [13•]	Baker's asthma [16]
α purothionin	Tri a 37 [6]	Severe anaphylaxis due to wheat [6]
α/β-gliadin	Tri a 21 [9]	WDEIA [7], wheat allergy [19]
γ-gliadin	Tri a 20 [10]	WDEIA [7], wheat allergy [19]
High-molecular weight (HMW) glutenin	Commonly composed of 3–5 subunits in wheat [14•]	WDEIA [8, 12, 20], wheat allergy [19]
Low-molecular weight (LMW) glutenin	Tri a 36 [15]	Wheat allergy [19]

were negative for specific IgE antibody to ω-5 gliadin [7]. 10/17 (59%) were positive for specific IgE to high-molecular weight HMW-glutenin, but this did not include the 3 negative patients for ω-5 gliadin [7]. 20 control subjects were not positive to any of the allergens tested by immuno-CAP or microarray [7].

In another study of 30 patients with WDEIA, 6/30 were found to have elevated specific IgE to HMW-glutenin, compared with 23/30 for ω-5 gliadin [8]. The investigators also tested synthetic epitope peptides of HMW-glutenin and ω-5 gliadin and found specific IgE against those proteins in 29/30 patients [8]. This finding raises the possibility of using synthetic epitopes in allergy diagnostics.

Additionally, the presence of ω-5-glaidin antibody has been proposed as an indicator for increased likelihood of experiencing a more severe reaction in wheat allergy. In one study of 88 wheat-sensitized children, the mean specific IgE antibody against ω-5-glaidin was found to be 7.25kU(A)/I in wheat allergic patients versus 1.08kU(A)/I in non-allergic ($p < 0.01$) patients. Eight children who had severe reactions had increased levels of specific IgE to ω-5-gliadin compared to children with no, mild, or moderate symptoms ($p < 0.001$) [14•].

In a follow-up study of the same 88 patients 2 years later, ω-5 gliadin was checked and found to be below 0.35kU(A)/L in 10 /15 who outgrew wheat allergy, and elevated with a mean of 5.89kU(A)/L) in 12/14 children with persistent wheat allergy.

Ebisawa et al showed that, in a study of 311 children and young adults suspected of wheat-related symptoms, the mean ω-5-gliadin was 1.2kU(A)/I in wheat-allergic patients versus <0.35kU(A)/I non-allergic patients ($p < 0.0001$). Positive and negative predictive values of (omega symbol)-5-gliadin in regards to predicting wheat allergy were 72% and 75% respectively [21].

Wheat allergy

Laurian et al. reviewed 36 studies, including over 250,000 adults and children, with the goal of determining food allergy prevalence. 21 of those studies estimated wheat allergy prevalence in the USA, Europe, and Australia. Four studies utilized food challenge testing to show a prevalence of wheat allergy of 0–0.5% (ages 3–14 years). Six studies employed skin prick testing which showed positive test results in 0.2–1.2%. Serum specific IgE was used in five studies with a prevalence of 0–3.6%, and six studies estimated prevalence based on patient or parent perception of allergy, with a reported prevalence of 0.2–1.3% [22].

Wheat allergy is more commonly outgrown compared with some other foods, such as peanut. This is consistent with the finding that about 85% of food hypersensitivity reactions in adults and adolescents are from shellfish, fish, tree nuts, and peanuts [2]. Specifically with wheat, one study showed resolution of allergy based on food challenge in 29%, 56%, and 65% of prior wheat allergic patients by ages 4, 8, and 12 respectively [23]. Median age of patients outgrowing their wheat allergy was about 6.5 years [23]. Discussing this can be helpful in aiding parents' expectations regarding their child's wheat allergy.

While wheat allergy bodes a less severe prognosis compared with peanut, for example, severe reactions including anaphylaxis to wheat have been known to occur [8, 12, 19, 24]. A US registry of food allergy-related fatalities can be found at https://www.nationalfoodallergydeathregistry.org/the-registry. This registry

has data starting from 1983 and lists over 100 deaths. One death is attributed to wheat in a 14-year-old in New Jersey in 2015. This single death is consistent with the general belief that wheat allergy is less dangerous than some of the other foods such as peanut or fish allergy; however, it also highlights that wheat allergy has the potential to be fatal [19].

One retrospective study by Cianferoni et al. investigated suspected wheat allergic patients at Children's Hospital of Philadelphia. 93 patients underwent oral food challenge (OFC) to wheat. 42% (39/93) of wheat challenges were positive. Wheat along with peanut challenges was noted as a risk factor for more severe anaphylaxis requiring IM epinephrine, including at a low dose of wheat [24]. Food challenge failure to wheat was associated with younger age, higher specific IgE, and smaller skin prick testing diameter. Smaller diameter and younger age were associated with necessity for intramuscular epinephrine [24]. Therefore, the authors concluded that food challenges to wheat should be performed in centers equipped to manage anaphylaxis and that small skin prick testing reactions should not necessarily be reassuring in young wheat allergic patients.

WDEIA

Practical measures for wheat allergy

Certain antigens, as above, have been associated with a particular type of wheat-associated anaphylaxis called wheat-dependent exercise-induced anaphylaxis (WDEIA). In 2016, Asaumi found wheat to be the most common food culprit in 20 patients with food-dependent exercise-induced anaphylaxis (FDEIA) [25]. WDEIA is a subset of exercise-induced anaphylaxis (EIA) when a patient develops an anaphylactic episode only if wheat is ingested followed by exercise within a few hours [26]. WDEIA may be suggested in the setting of EIA with a positive serum or scratch test to wheat. The gold standard for diagnosis for FDEIA is an exercise challenge after food ingestion. Symptoms are known to occur during exercise [27], and it is believed that 80% of reactions of FDEIA happen within 2 h of eating the suspect food [27]. One episode of WDEIA, however, was reported in a 16-year-old patient who lost consciousness 5 h after playing 1 h of basketball. His percutaneous skin test was positive to only wheat (4+) [28]. So, it appears that delayed reactions are possible in WDEIA. Figure 1 illustrates the main features of FDEIA.

Comorbid asthma is common in FDEIA along with prior positive skin prick tests to the culprit food. Some patients with WDEIA could even have a history of reacting to the wheat food in the past. In terms of incidence, it appears that the incidence of FDEIA anaphylaxis is increasing. It has roughly a 2:1 female predominance, and is most common in the late teens to mid-thirties [2].

Lastly, a subset of WDEIA patients has been described who used a certain soap that contained hydrolyzed wheat (HWP). They were noted to have first developed contact allergy and then proceed to manifest WDEIA later [29]. Others that used this soap did not develop WDEIA but developed symptoms simply after wheat ingestion. This subset of WDEIA patients was not appreciated to have a significant elevation of ω-5 gliadin antibodies [29]. As in this case and in oat allergy discussed later, it seems reasonable to recommend against

Fig. 1. Features of food-dependent exercise-induced anaphylaxis (FDEIA).

patients using grain containing skin-contacting products, especially in patients with eczema.

The exact mechanism by which wheat or any other foods influence an episode of exercise-induced anaphylaxis is not fully understood [2]. It is believed, however, that either aspirin or exercise help allergen uptake from the gastrointestinal tract thus leading to increased symptomatology in FDEIA [12, 30].

Helping patients and caregivers to identify food sources that contain wheat which could be important in avoiding potential reactions. Some less obvious sources of wheat include ale, beer, hot dogs/processed meats, candies, soy sauce, surimi, gravy, soups, salad dressings, and ice cream products. Severe wheat allergy can come with significant life style changes and can place a significant limitation on a patient's diet. It can be helpful to provide patients with foods that are felt to be safe in wheat allergy. Such foods include rice, corn, barley, oat, soybean, potato, quinoa, millet, buckwheat, amaranth, tapioca, and arrowroot [31].

In looking at anaphylaxis due to any food, including cereals, it is important to differentiate reactions to the food that do not represent anaphylaxis. Some wheat-related conditions are not IgE mediated, and anaphylaxis from these conditions is not likely. These health issues include food protein-induced enterocolitis syndrome (FPIES), eosinophilic esophagitis (EoE), eosinophilic gastritis/enterocolitis/colitis, baker's asthma, and celiac disease. Since these conditions may be worsened by wheat exposure, they are important to consider in a patient who presents with "wheat allergy".

In conclusion, wheat allergy can cause significant morbidity and can be associated with anaphylaxis due to ingestion or in the setting of WDEIA. The

elucidation of wheat antigens has provided the possibility for aiding in diagnosis and prognosis of wheat related allergy. Practical counseling of patients who experience wheat-induced anaphylaxis regarding foods to avoid and foods that are safe is recommended.

Oat

Oat allergy prevalence was estimated with a prospective study of 302 children with atopic dermatitis (AD) who were submitted to patch testing and skin prick testing to oat which found sensitization in 15% and 19% of patients respectively. Oral food challenge to oat was done in these sensitized patients and was found to be positive in 15% or 5/32 (5/302 or 1.7%). Patch testing was positive in 32% of patients who had used oat-based skin cream and 0% positive in those who did not use an oat product on the skin [32].

Anaphylaxis to oat has been reported from patients sensitized to oat from both the oral and cutaneous routes [33, 34]. The latter was seen in a 30-year-old woman with history of adult onset eczema who treated herself with a moisturizing agent that contained oatmeal. She later experienced shortness of breath from aerosolized oatmeal, and after that had an anaphylactic reaction to apple crumble. She was found to have an oat specific IgE level of 84.2kU/L. Basophil activation test was consistent with allergic sensitization to oat. It was hypothesized that she became sensitized through the broken skin barrier caused by eczema [33].

Anaphylaxis to oat due to GI sensitization was manifested by a 23-year-old woman found to have a significantly elevated oat specific IgE (>100UA/ml) and positive skin prick test. She was felt to have been sensitized to oat via the gastrointestinal route rather than the skin, as she had no known history of skin care product containing oats. Interestingly, the patient had a wheat specific IgE of 71.1 UA/ml (class 5) and positive skin prick test to wheat without any clinical reaction to wheat [34].

It is important to note that contact urticaria has occurred with emollient cream containing oat [35], which would not represent anaphylaxis but could potentially be confused with anaphylaxis. Contact dermatitis, confirmed by patch testing, has been seen with oat containing products even without food reaction [36].

Overall, oat food allergy is relatively uncommon; however, it has been known to cause anaphylaxis. Given the potential for sensitization via the skin route with topical treatments containing oat for eczema patients, these products should not be recommended; good moisturizing agents for the treatment of eczema exist that do not carry this risk.

Barley

Barley is the major grain used in the brewing of beer. It is usually malted barley which means the barley was soaked, germinating the grain; other grains, hops, and yeast can be added [37]. It is widely known that beer and other alcoholic beverages can augment reactions to food; however, allergic reactions to beer itself are not as commonly reported [38]. Anaphylaxis has been reported to the beer itself, and more specifically to the barley in the beer [38–40].

One episode of beer-related anaphylaxis was evaluated and found that the patient had skin prick test positivity to barley, and also to corn and wheat [41]. Thus, in the evaluation of suspected reactions to the actual beer, evaluation of the different potential components (barley, wheat, etc.) is prudent.

Aside from beer, anaphylaxis can occur via oral ingestion of barley cereal [40]. This was manifested by a case of anaphylaxis to barley that was reported in an infant who consumed weaning food that contained barley. The patient experienced dyspnea, periorbital swelling, urticaria, and wheezing, and was found to have high levels of specific IgE to wheat and barley. High level of IgE cross-reactivity between wheat and barley extracts from IgE-immunoblot inhibition and ELISA-inhibition testing was noted [42].

Palosuo et al. studied sera of 23 patients with WDEIA. As mentioned earlier, ω-5 gliadin antibodies are important in WDEIA [12]. In this study the authors looked for cross-reactivity between ω-5 gliadin and allergens in barley, rye, and oats. Cross-reacting allergens were identified using immunoblot inhibition, then further studied with gel filtration, reverse-phase chromatography, amino acid sequencing, IgE ELISA, ELISA inhibition, and in vivo skin prick testing. Barley γ-3 hordein, rye ω-35 secalin, and rye ω-70 secalin were found to cross-react with ω-5 gliadin, raising the concern that rye and barley could be problematic in patients with WDEIA, and skin prick testing and/or avoidance of barley and rye could reasonably be pursued. No cross-reactive protein was found with oat [43].

Rye

It was noted above that rye antigens ϒ-35 secalin and ϒ-70 secalin cross-react with the wheat antigen ω-5 gliadin [43]. This suggests that is reasonable to perform an oral challenge to rye or recommend avoidance of rye in patients with WDEIA.

A rye-dependent exercise-induced episode of anaphylaxis was reported in a 61-year-old woman with allergic rhinoconjunctivitis with no prior food allergy history. She consumed toasted rye, then took acetylsalicylic acid and walked for 30 min. An hour after she ate the toasted rye, she developed anaphylaxis. She was found to have elevated specific IgE to rye (5.71 kU/L) but also to wheat (9.54kU/L), ω-5 gliadin (19.5kU/L), barley (1.69 kU/L), oat (0.89 kU/L), maize (1.93 kU/L), and rice (2.68 kU/L). She avoided rye and other grains with the exception of wheat. Also, she was instructed against the use of NSAIDs or exercise for 4 h after wheat ingestion. Two years later, she took 2 tablets of streptokinase-streptodornase and consumed wheat without exercising and developed diffuse urticaria [37].

Millet

In 1981, Parker et al. reported a case of anaphylaxis to millet after eating date-millet pudding. Intradermal skin testing was positive to millet at lower concentration compared to two control subjects. RAST inhibition assays were used to look for cross-reactivity between millet seed, grasses and other grains (barley, oat, rye, wheat, rye grass, June grass, orchard grass pollen); however none was found [44]. Another case reported in 2020 describes a 59-year-old Japanese

woman who was found to have WDEIA and elevated anti-ω-5 gliadin-IgE. Although instructed to avoid wheat products, she developed anaphylactic shock 20 min following noodle ingestion that was wheat-free but contained millet. Notably, she had fed a budgerigar millet containing birdseed in her bedroom since the age of 43. Skin prick testing was positive for wheat, bread, and birdseed, and also showed significant reactions to foxtail and Japanese millet. The foxtail and Japanese millet were the main ingredients in the birdseed she had used to feed her budgerigar. Competitive western blotting was done and indicated that all the IgE-binding determinants in wheat were present in millet but that the reverse was not true. It was thus believed she was primarily sensitized to millet, and that some of the patient's anti-millet IgE antibodies cross-reacted with wheat antigens [45]. Another case from 2015 reported anaphylaxis to millet with a possible exercise component (in the form of a strenuous walk) [46].

The major prolamin in millet is panicin, but this has not been proven to cross-react with ω-5-gliadin [46]. Hemmer et al. looked at 9 adult patients who had convincing history of allergy to millet. Interestingly, 8 of the 9 were either former or current keepers of budgerigars which were routinely fed millet (birdseed mixture or foxtail millet). 4 of those 8 were exposed to the birds only during childhood. Positive specific IgE to millet was found in 8/9, to corn in 7/9, wheat 6/9, and rice 6/9. IgE to millet was the highest in 8/9 patients. The last patient showed stronger binding to sesame. IgE binding inhibition testing revealed cross-reactivity between millet-primary sensitized patients to rice antigen [47].

Consistent with the last report, Bohle et al. described seven patients who kept birds in cages who developed reactions after ingestion of millet [48]. It appears bird keeping is a risk factor for millet sensitization and anaphylaxis.

Corn

A case of FDEIA due to corn, confirmed by exercise challenge 40 min after eating taco chips, was reported. The patient was instructed to avoid corn, and carry epinephrine. Later, the patient developed anaphylaxis to corn without any exercise. Interestingly, she had a large positive skin prick to wheat, although she could eat wheat without problem [49].

In a prior noted study, barley and corn ingredients were implicated in beer induced anaphylaxis [39]. So, corn allergy should be considered a possibility in cases of beer induced anaphylaxis.

Anaphylaxis has also resulted from topical corn exposure. A patient had used a soap containing corn for about 3 months. After 9 months of abstaining from the soap, it was used again, and anaphylaxis developed within 30 min. Twenty days afterward, the patient had lip swelling after eating a snack with corn. It was believed she was sensitized through the cutaneous route associated with the soap. The patient was found to have elevated specific IgE to millet in addition to corn, however the patient had never had millet and this was believed to represent cross-reactivity between corn and millet. The patient did not have further episodes after avoiding corn [50].

Rice

Rice is the seed of the plant *Oryza sativa*, and is the second most produced grain behind maize (corn) in the world (Food and Agriculture Organization of the United Nations (FAO): International Year of Rice: 2004. Rice is life. Fact sheets (http:// www.fao.org/rice2004/en/factsheets.htm)). Despite the widespread use of rice, rice allergy via IgE mediated hypersensitivity is quite rare [51]. In addition to ingestion reactions, a reaction to rice via inhalation from nearby rice manipulation has been reported [52]. A case of near fatal anaphylaxis to rice inhalation when rice was being cooked was reported in an 8-year-old boy with rice sensitization [53]. Contact urticaria from washing rice, without symptoms after eating cooked rice, has also been reported [54], which would not represent anaphylaxis. In addition, asthma symptoms, rhinoconjunctivitis, and contact urticaria were reported from handling rice, without clinical symptoms from ingesting cooked rice [55]. Anaphylaxis to cooked rice has been reported [51, 56] as well as bronchial asthma attacks from rice [57]. Rice allergy, while rare, can cause a wide range of manifestations including anaphylaxis, and reactions similar to anaphylaxis, such as asthma exacerbation or urticaria.

Cross-reactivity

Cross-reactivity has been shown between ω-5 gliadin of wheat and rye and barley antigens [43]. Cross-reactivity between millet and wheat has been demonstrated [44], and there is some evidence for millet and rice cross-reactivity [47]. Lastly, there is questionable evidence of cross-reactivity between corn and rice [49]. The question could be asked as to whether patients with WDEIA or FDEIA to a specific cereal should be evaluated for allergy to all cereals upon diagnosis? It could be argued that skin testing is relatively easy and inexpensive, and may allow for safe introduction of cereals with a negative result, while also providing for guidance on which cereals to avoid or perform a challenge. Table 2 shows cereals known to cause FDEIA and potential cross-reactivity.

Cereal contamination

Cereal contamination is an important consideration in cases of anaphylaxis following grain ingestion. This possibility should be especially considered if skin and or specific IgE testing to cereals is negative. A recent case was reported of anaphylaxis after eating oat and rice containing meals. With negative testing to the cereals, further investigation revealed hypersensitivity to the insect *Liposcelis bostryochophilia* that had contaminated both oats and rice. This insect is the most common book lice species and can be found in granaries, kitchens, and flour mills worldwide. Stored food, including cereal, can commonly be infested by this organism [58].

Additionally, in 1993, Erben et al. reported a case of anaphylaxis subsequent to eating homemade beignets. The patient was significantly sensitized to house

Table 2. Cereal causes of food-dependent exercise-induced anaphylaxis

Cereal	Potential cross-reactivity	Important antigens involved
Wheat [4•, 7, 8, 12, 25, 28, 29]	Barley [43], rye [37], and millet [45]	ω-5-gliadin [37]
Barley [42]	Wheat [43] and rye [37]	γ-3 hordein [37]
Rye [44]	Barley [37] and wheat [43]	γ-35 secaline [43] and γ-70 secalin [43]
Corn [50]	Millet [50]	
Millet [47]	Wheat [46] and rice [48]	

dust mite and his beignet mix was found to be mite infested [59]. Blanco et al. prospectively confirmed that a number of patients had systemic reactions to challenges with dust mite contaminated flour [60]. Anaphylaxis from oral ingestion of dust mite is more common in tropical environments, and can be caused by pancakes and has been even called "the pancake syndrome" [61•]. Thus, the consideration of flour contamination should be considered in the differential diagnosis of cereal allergy/anaphylaxis. Advising patients who are strongly allergic to dust mite to keep fresh flour, and dispose of flour that has been stored long-term in a pantry, is a reasonable recommendation.

Diagnosis

To diagnose anaphylaxis due to cereal, as with any food, a thorough history is the most critical component. Discerning involvement of at least two organ systems (skin-GI, skin-respiratory, etc.) within a few hours after ingestion of cereal supports the diagnosis. Confirmatory cereal specific IgE antibodies detected in the serum or by skin prick testing are highly recommended. Commercial extracts to certain cereals may not be available, so prick-to-prick testing is considered a viable alternative.

Treatment

Current standard of care in patients with cereal anaphylaxis is strict food avoidance and intra-muscular epinephrine as needed for reactions. All such patients with history of anaphylaxis need to be given a(n) epinephrine auto-injector(s), preferably two; a second injection can be given 5–15 min after the first dose, if needed. Patients should have an injector available at school if applicable. Proper injector technique should be taught to the patient/caregiver; confidence in its use could prove very important in a high stress moment. Finally, epinephrine usage should prompt the patient to seek emergency care immediately for further observation and treatment if needed.

With the emergence of oral immunotherapy for other foods, such as peanut, oral immunotherapy for wheat-induced anaphylaxis has been introduced in recent years. One group took patients with double blind food challenge proven anaphylaxis to wheat, and showed that wheat oral immunotherapy taken by 18 patients (11 controls) over 2 years induced tolerance in 60% of patients [62]. In the USA, there is not a standardized FDA approved product available, but

certain practitioners have developed novel protocols for homemade wheat immunotherapy, and reported some success.

Conclusion

Allergies to cereal grains while less common, are known to cause severe reactions, including anaphylaxis. This anaphylactic reaction can occur after ingestion or alternatively ingestion temporally related to exercise. Important potential cross-reactivities between different cereal grains has been shown, and clinically would be important in cases of anaphylaxis. Cereal contamination is another important entity when considering anaphylaxis after cereal ingestion. Although wheat immunotherapy has been undertaken, the standard of care at this time is culprit avoidance, epinephrine auto-injector prescription, counseling, and follow-up.

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