

Wheat-dependent exercise-induced anaphylaxis: Are you sure about the diagnosis?



Christensen et al¹ conducted an interesting study to offer a practical approach in wheat-dependent exercise-induced anaphylaxis (WDEIA) diagnosis. Their proposed challenge algorithm substantially increased the sensitivity of testing, at least in their hospital setting, and sounds promising and generalizable. In addition to this very important finding, Christensen et al proved that ω -5 gliadin-associated regular wheat allergy is highly dose dependent under normal conditions and that the WDEIA diagnosis has been erroneously ascribed to many of those initially diagnosed with this entity. The fact that exercise can unmask the underlying regular allergy when these patients are challenged with high doses of gluten is valuable information with clinical implications, especially for the testing procedures and advice about prophylaxis against reactions. In this context, it might not be correct to state that “Wheat-Dependent Exercise-Induced Anaphylaxis can be elicited at rest.” By definition, WDEIA occurs only when the patient exercises within 2 to 4 hours of ingesting wheat, but in the absence of exercise, the patient can ingest wheat without any apparent reaction. In the case of an allergic reaction without exercise, the diagnosis is regular food allergy to wheat.

In line with the dose-dependent finding, it would have been of interest to challenge individuals sensitized to ω -5 gliadin (but tolerant to it under any circumstances) with these unphysiologically high amounts of gluten with or without exercise to examine whether these asymptomatic patients could become symptomatic. And, of course, it remains to be examined whether other allergens contained in foods that have been associated with food-dependent exercise-induced anaphylaxis can elicit food allergy symptoms at rest, if administered in high amounts.

Another wheat allergen of great importance is Tri a 14. Tri a 14 belongs to the lipid transfer protein (LTP) family and is found in the wheat kernel. Although Tri a 14 has been reported to be a major allergen associated with baker's asthma, it also seems to be important in regular wheat allergy. In an Italian study, almost half (9 of 22),² and in a similar French study a third (17 of 60) of the examined wheat allergic individuals were sensitized to this allergen.³ Because the clinical expression of LTP allergy often requires one or more cofactors,^{4,5} it may be of interest to measure specific IgE levels to Tri a 14 in all individuals with a history suggestive of wheat allergy, so that potentially associated LTP allergy, which often requires one or more cofactors to be induced (eg, exercise, nonsteroidal anti-inflammatory drugs, or alcohol), can be identified.

Last but not least, another parameter to be considered is that the high amount of gluten was given to the patients on an empty stomach. There is evidence suggesting that the isolated ingestion of the culprit food allergen after fasting may be the only necessary and sufficient condition for the allergic symptomatology to emerge. This observation has been noted for LTP-allergic individuals, but may apply to other allergens as well.⁶

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Reply



To the Editor:

Konstantinou¹ comments on some interesting points regarding our study.² Our objective was primarily to confirm the diagnosis and establish a reliable challenge method. The acronym WDEIA (wheat-dependent, exercise-induced anaphylaxis) is probably not precise and may be outdated, because exercise is not mandatory,³⁻⁶ but by far the most common reported cofactor in food allergy.⁷ Because other cofactors such as aspirin and alcohol also are involved,³ the correct term in the future might be wheat-dependent, cofactor-induced anaphylaxis. We have results upcoming to support this hypothesis. However, until then, the term WDEIA is well established and best describes the reaction patterns described by the patients in their history.

The reaction during exercise is probably elicited by a combination of wheat ingestion and an increase in metabolism or absorption. If a high level of metabolism or absorption is taking place (strenuous exercise), the amount of gluten necessary to elicit a reaction is low, and vice versa at rest, where a very high amount of gluten is necessary. From a semantic point of view, these patients might be classified as merely wheat allergic, but this would confuse the traditional definition of classical wheat allergy (in children) being elicited by water-soluble allergens and would not reflect the fact that all of the patients reported reactions primarily or exclusively together with cofactors, particularly exercise. The amounts of gluten given during our challenges correspond to higher levels of omega-5-gliadin than present in the

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