



Food-Dependent Exercise-Induced Anaphylaxis: A Review

Cze-Ja Tam, MSN, CPNP-PC, and Rita Marie John, EdD, DNP, CPNP

ABSTRACT

Food-dependent exercise-induced anaphylaxis (FDEIA), a subtype of exercise-induced anaphylaxis (EIA), is underdiagnosed and unreported. FDEIA is unpredictable and difficult to diagnose because its manifestation relies on the presence of several modifiable factors but can be fatal for the individual if not properly assessed and treated. A proper diagnosis of FDEIA will help prevent unnecessary food and exercise limitations and provide a patient with FDEIA an adaptable lifestyle. The purpose of this article is to review FDEIA characteristics, diagnostic tools, management, and the role of the nurse practitioner in diagnosing and caring for children or adolescents with suspected FDEIA.

Keywords: allergy, anaphylaxis, food-dependent exercise-induced anaphylaxis, immunology, pediatric primary care, urgent care

© 2017 Elsevier Inc. All rights reserved.

Both authors are affiliate with Columbia University School of Nursing in New York, NY. Cze-Ja Tam, MSN, CPNP-PC, is a certified pediatric nurse practitioner and can be reached at czejatam@gmail.com. Rita Marie John, EdD, DNP, CPNP, is an associate professor of nursing at CUMC; and a director of the pediatric primary care nurse practitioner program. In compliance with national ethical guidelines, the authors report no relationships with business or industry that would pose a conflict.

A 17-year-old female Chinese high school student (N.C.) had 3 episodes of severe allergic reactions to shrimp consumed before exercise over 2 years. Before her first episode, shrimp was part of her monthly diet. After playing tennis and 45 minutes after ingestion of shrimp, N.C. developed widespread urticaria, swelling of her fingertips and toes, and total vision loss for 5 minutes while conscious. Although antihistamines helped decrease the swelling and pruritus over a few hours, the episode was frightening. Over the next few years, she noticed if she did not exercise, she could consume shrimp without reactions.

At 19 years old, immediately after eating shrimp, she moved heavy boxes. Within 1 hour, N.C. developed extensive hives followed by significant facial edema, especially of her left eye. While her fingertips, toes, and tongue were swelling, N.C. was given an antihistamine and epinephrine injection. She was diagnosed with a shellfish allergy. This diagnosis did not consider other possibilities like food-dependent exercise-induced anaphylaxis (FDEIA). Individuals with FDEIA are often misdiagnosed with food allergy only, and FDEIA is overlooked. This article discusses the pathophysiology, epidemiology, possible triggers, and

This CE learning activity is designed to augment the knowledge, skills, and attitudes of nurse practitioners and assist in their understanding of diagnosis and treatment of food-dependent exercise-induced anaphylaxis (FDEIA).

At the conclusion of this activity, the participant will be able to:

- List possible triggers and cofactors of possible triggers of FDEIA.
- Identify the clinical presentation and diagnostic work up of a patient with FDEIA.
- Identify the management of FDEIA by the NP.

The authors, reviewers, editors, and nurse planners all report no financial relationships that would pose a conflict of interest. The authors do not present any off-label or non-FDA-approved recommendations for treatment.

This activity has been awarded 1.0 Contact Hours of which 0.5 credit are in the area of Pharmacology. The activity is valid for CE credit until June 1, 2019.

differential diagnoses of FDEIA and the role of the nurse practitioner (NP) in managing FDEIA and preventing impending anaphylaxis.

OVERVIEW

FDEIA is a subtype of exercise-induced anaphylaxis (EIA). FDEIA is an immunoglobulin E (IgE)-mediated hypersensitivity reaction to food allergens and usually occurs when exercise is preceded by the ingestion of the putative food.¹ The severity of EIA symptoms may vary, and fatalities are uncommon, with a mortality estimate of 1 in every 1,000 cases.² FDEIA can be specific, in which a specific food allergen triggers FDEIA, or nonspecific, in which severe symptoms occur with the ingestion of any food preceding exercise.³

Maulitz et al⁴ reported the first case of food hypersensitivity after strenuous exercise in which a 31-year-old man had anaphylaxis only when ingesting shellfish before exercising.⁴ In 1983, researchers termed this condition FDEIA after studying cases of exercise-induced anaphylaxis from celery ingestion.⁵ Further research confirmed that in patients with FDEIA the food allergen and exercise could be tolerated independently.⁶ Although several foods have been reported to be associated with FDEIA, the most commonly studied culprit food of FDEIA is wheat. The first case of wheat-associated exercise reaction was reported in Japan and was called wheat-dependent exercise-induced allergy (WDEIA, a subtype of FDEIA).⁷ Since these first few case reports, several foods have been associated with FDEIA, and there is a possible geographic variation.³

Prevalence

The prevalence data of FDEIA are limited and not accurately reported.⁸ The majority of reported cases have been wheat related.⁸ The reported prevalence has ranged from < 0.001% to 0.017% worldwide for all food.⁹ FDEIA remains often underreported, with only 700 cases studied and recognized in the world.¹ According to Du Toit,¹⁰ 5% to 15% of anaphylaxis cases are caused by EIA, and of the EIA patients, 33% to 50% have FDEIA.¹⁰ Most studies state that FDEIA appears to be twice as common in males as in females with the highest prevalence

between the teenage years and 35 years old;¹¹ however, it occurs at a lower rate in children, likely because of unreported cases.¹¹ Although many cases are often unreported, Flannagan and Wolf¹² describe 1 fatal incident in which a patient collapsed after ingesting hazelnuts and almonds before vigorous dancing.

Food Triggers. FDEIA has 2 subtypes: specific FDEIA, in which ingesting a particular food allergen before exercise induces anaphylaxis, and nonspecific FDEIA, in which any food preceding exercise causes EIA.¹³ Several foods have been associated with FDEIA; wheat, shellfish, and nuts are noted as the most common food triggers.⁷ Other food categories of less commonly reported FDEIA triggers include protein meat, vegetables, fruit, seeds, and cereals.¹⁰ The omega-5 gliadin, a component of wheat, was the main allergen in individuals with FDEIA. With more research, additional plant and animal proteins have been added to this list, including rice and tomatoes.¹⁴

Exercise Triggers. The types and intensity of physical exercise that impact FDEIA vary for each individual. FDEIA has been detected in both well-trained athletes and individuals partaking in occasional exercises like walking.¹⁵ Both strenuous and light exercise can induce anaphylaxis after ingestion of the causative food.¹⁶ Specifically in FDEIA, the time between food ingestion and exercise has been 30 to 120 minutes, and symptoms do not present until after an exercise duration of at least 10 to 50 minutes.¹¹

Cofactors. In some cases, studies reported that cofactors are required for developing a reaction in FDEIA patients. Some types of noted cofactors include aspirin,¹⁷ cold environment,¹⁸ warm environment and high humidity,^{18,19} atopic dermatitis,²⁰ alcohol intake,²¹ and menstrual cycle.²² In temperature-related cases, researchers gathered evidence that some patients with FDEIA only had FDEIA symptoms if they were in cold, warm, or humid environments; without the exact temperature and humidity trigger, FDEIA symptoms were not present.^{18,19} Gonzalez-Quintela et al²¹ reported that alcohol ingestion can trigger high levels of total blood IgE levels. There can be multiple combined triggers as shown in a case report in which FDEIA symptoms occurred after ingesting

cow's milk, aspirin, and exercise during her ovulatory and premenstrual phase.²²

Clinical Manifestations. Clinical manifestations of FDEIA resemble the typical presentation of anaphylaxis. FDEIA generally progresses from skin manifestations to loss of consciousness or dyspnea.¹⁵ Skin symptoms may or may not include generalized urticaria, angioedema, and/or erythema. Respiratory manifestations include dyspnea, coughing, or wheezing. Abdominal pain, fatigue, and hypotension are all possible. Symptoms vary depending on the amount of ingested culprit food, intensity of exercise, and sensitivity of the immune system.¹⁶ The [Figure 1](#) provides a review of anaphylaxis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis is challenging. The provider must consider *exercise-related* diagnoses in addition to *exercise-induced* diagnoses²³ and distinguish anaphylaxis from less severe reactions. Food allergies can either be distinguished as delayed cell mediated (type IV allergic reactions) or IgE mediated (type 1 allergic reactions). [Table 1](#) outlines the common differential diagnosis and their clinical presentation. Although there may be several cofactors causing anaphylaxis, exercise can also be a cofactor in worsening an existing allergy as exercise related, rather than being the cause of anaphylaxis. The provider must consider all possible differentials before suggesting FDEIA.

PATHOPHYSIOLOGY

The pathogenesis of FDEIA is not clear, but there have been several hypotheses proposed to explain FDEIA. Ring et al²⁴ described a *summation anaphylaxis* phenomenon wherein FDEIA includes both IgE-mediated and non-IgE-mediated reactions.²⁴ Robson-Ansley and Toit¹⁵ suggested that during exercise blood is shunted from vital organs to the musculature and skin, causing recently ingested food allergens to be displaced from their usual sites of absorption in the gut and increasing the chance of anaphylaxis. Researchers proposed that there is increased gastric permeability during physical activity, which allows the allergenic

proteins greater access to the gut-associated immune system.²⁵ A third hypothesis involves alterations in the plasma pH in which strenuous physical activity triggers mast cell degranulation.¹⁵ Another proposed pathogenesis suggested that the increased activity stimulates the tissue transglutaminase enzyme, which may cause increased IgE cross-linking because of peptide aggregation.²⁶ Researchers demonstrated in their study that FDEIA might be a result of exercise-induced changes in the plasma osmolality.¹⁸ Cooper et al²⁷ explored the possible explanation of FDEIA as the activation of circulating leukocytes, which stimulate and prolong the proinflammatory response during exercise. None of the proposed mechanisms have enough research to solidify the pathophysiology of FDEIA.

DIAGNOSIS

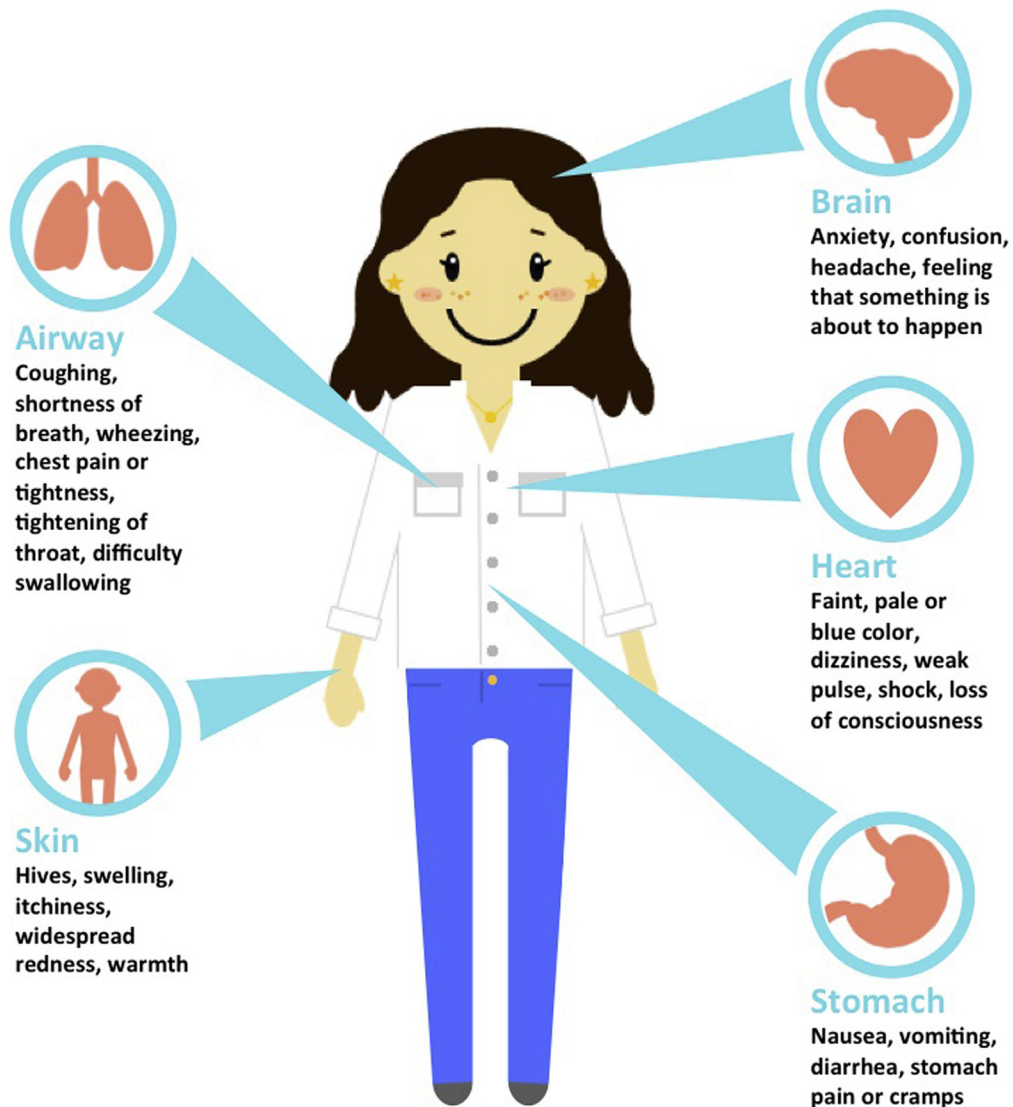
Because FDEIA is predominantly a clinical diagnosis, a thorough history is key. A careful medical history and identification of the events precipitating the reaction and the involved cofactors must be considered when gathering the individual's history. It is important to rule out any possible food-induced allergic reactions.²⁸ Although researchers noted that most children with FDEIA may manifest symptoms only by 1 specific food allergen,²⁸ several studies have provided evidence that some may have multiple food triggers.^{29,30} [Table 2](#) provides questions to obtain a complete history.

A diagnosis of FDEIA can be made clinically by following the World Allergy Organization criteria for WDEIA because it is merely a subtype of FDEIA and has a similar presentation. [Table 3](#) outlines these criteria.³¹ Guidelines for diagnosing WDEIA can be adapted to food-specific FDEIA.

If a patient actively presents with anaphylaxis, a complete physical examination is warranted. For instance, if wheezing were present, this would be a critical finding to determine whether or not wheezing is associated with FDEIA or exercise-induced asthma.²³ Several studies have shown that children with suspected EIA or FDEIA have a history of atopic dermatitis.^{2,29}

Figure 1. Signs and symptoms of anaphylaxis. This worksheet is available for providers to distribute to their patients and families.

SIGNS and SYMPTOMS of ANAPHYLAXIS



GIVE  **EPINEPHRINE**

&

CALL 

Table 1. Differential Diagnoses of Food-dependent Exercise-induced Anaphylaxis

Diagnosis	Signs and Symptoms
Exercise-induced anaphylaxis	Flushing, generalized pruritus, a feeling of warmth, and urticaria during exercise with the absence of a food trigger
Food hypersensitivity	Cell-mediated (delayed): 2 to 3 days for reaction to develop; allergic contact dermatitis Immunoglobulin E mediated (acute): urticaria, pruritus, angioedema, and eczema
Mastocytosis	Presence of urticaria pigmentosa
Hereditary angioedema	During exercise, hereditary angioedema may evolve without urticaria ¹⁰ ; edema of hands, feet, face, gastrointestinal tract, genitals, and larynx
Cholinergic urticaria	Urticaria occurs when increased cholinergic activity or the body experiences extreme exertion, for instance, sweating during exercise or in hot environments ¹
Cold urticarial	Urticaria because of the cold environment
Exercise-induced asthma	Bronchospasms, wheezing, coughing

Allergy Testing

Double-blind Placebo-controlled Food

Exercise Challenge. Several diagnostic tests are available to confirm FDEIA, but the gold standard of FDEIA would be a double-blind placebo-controlled food exercise challenge (DBPCFEC). It is used when symptoms are unusual or ambiguous.^{29,32} Fiochhi et al³² were the first to use a DBPCFEC to diagnose FDEIA. This challenge test consists of 3 parts. Before testing, patients are encouraged to eliminate the suspect allergen from his or her diet for at least 2 weeks to prevent interference with the study.³³ Part 1 involves the food challenge alone to rule out the

need for exercise to induce the anaphylaxis.¹⁶ If a suspected food were unknown, a broad food panel would be used. In part 2, an exercise challenge is administered alone. In children, for the exercise challenge, the protocol is similar to that of exercise-induced bronchoconstriction; for at least 6 minutes, children perform an exertion continuously until they reach 80% maximum heart frequency.³⁴ In part 3, the food and exercise challenge are combined, with the patient ingesting the culprit food or placebo and exercising on a treadmill with the Bruce protocol in which the individual works to complete exhaustion to evaluate cardiac function.²⁹ In this challenge, to

Table 2. Allergy Questions for Diagnosing Food-dependent Exercise-induced Anaphylaxis (FDEIA)

Questions seek to establish
What are the presenting symptoms? Make sure that exercise or exertion occurred with every episode. Is a particular food ingested before each episode of symptoms? Did the patient ever get symptoms without eating any food?
Most reactions occur within 2 hours of eating so the patient may need to ask other people about the timing of the anaphylaxis related to food. A diary can be helpful if this is the first time the child ever had anaphylaxis.
What foods/drinks/supplements did the patient take before the episode? Does the patient feel that a food may have triggered the episode?
What medications do the patient take daily? Did he or she take any other medications before the episode? Do the symptoms change according to the time of the year? It is important to remember that inhalation and contact with food allergens are generally not enough because a significant amount is usually needed.
Is there a prior history of tolerance to the food (and cross-reacting allergens) because patients with FDEIA can tolerate the food in the absence of exercise?
Does the patient have other allergic diseases such as urticaria, allergic rhinitis, or asthma? Does he or she take medications for the disease because poorly controlled diseases can increase the patient's risk? ³⁵
Are there additional precipitating factors such as alcohol or nonsteroidal anti-inflammatory drug use?

Table 3. Food-dependent Exercise-induced Anaphylaxis Diagnostic Criteria

Criterion	Details
1) Anaphylaxis	Anaphylaxis after ingestion of food before exercise (urticaria, angioedema, and shortness of breath) Exercise must be within 4 hours of food consumption
2) Culprit food and exercise tolerated independently	Culprit food tolerated safely without exercise Exercise tolerated safely in the absence of culprit food ingestion

eliminate bias, neither the physician nor the patient are aware of what the patient is being fed. A diagnosis of FDEIA is confirmed if the results are positive when allergic symptoms are present, but if the challenge results are negative, FDEIA should still not be excluded as a diagnosis.³⁵ In some cases, anaphylaxis is only induced depending on whether there was a sufficient amount of food allergen ingested.³⁴ Because DBPCFEC can potentially induce anaphylaxis, there are medical-legal concerns. Because the test has not been universally validated and can induce anaphylaxis, the risk of death is a deterrent. Therefore, DBPCFEC may be deferred if the patient has a clinical history suggestive of FDEIA and a positive serum IgE antibody test.³⁶ The evaluation of FDEIA is not standardized, and DBPCFEC is not required to diagnose FDEIA. If it is done, the facility must be fully equipped to manage anaphylaxis. Other alternative nonspecific testing includes skin tests to identify the causative allergen and *in vitro* tests to identify the amount of specific IgE present. Table 4 reviews these tests.

MANAGEMENT OF FDEIA

Avoiding physical activity can be difficult and is not recommended for children and adolescents. It is critical for patients to avoid ingesting the culprit foods to reduce the likelihood of an FDEIA episode. If identification of the putative food is known, dietary changes regarding the timing of intake must be done to prevent anaphylaxis. Consulting a registered dietician for dietary changes is important.²⁸ Individuals with FDEIA should avoid the culprit allergen at least 4 hours before exercise and 1 hour after exercise. Waiting 1 hour after exercise is necessary for the recovery of blood flow.²³ As long as the patient does not exercise after eating the allergen, there is no need

to eliminate exercise or the culprit allergen from an individual's daily routine.

Proper diagnosis and management by the provider will help prevent unnecessary limitations on the patient's diet and exercise.³⁶ Patients should wear a medical bracelet as well as carry prescribed duo self-injectable adrenaline pens and antihistamines in case of accidental exposure during light or vigorous exercise.³¹ When exercising, the individual with FDEIA should have a friend or family member who understands FDEIA and how to administer epinephrine present in case of emergency.

When anaphylaxis occurs, emergency treatment is identical to that of IgE-mediated allergic reactions.³¹ If a patient is exhibiting signs of anaphylaxis, first administer an intramuscular injection of adrenaline (epinephrine) in the mid-outer thigh and then position the patient supine, or if he or she is dyspneic or vomiting, place the patient in a semireclining position. Antihistamines may be used to relieve urticaria and pruritus but should never be used to treat anaphylaxis as first line.³¹ The 911 system should be activated in order to provide supplemental oxygen, cardiopulmonary resuscitation, and intravenous fluid resuscitation and to monitor vital signs and oxygenation. If and when an individual is unresponsive, epinephrine doses can be repeated every 5 to 10 minutes until the individual is resuscitated. If a patient with FDEIA has underlying asthma, corticosteroids and an albuterol inhaler must also be available in case of emergency but should not be given for anaphylaxis before adrenaline even if the patient presents with wheezing.³¹ When an individual is diagnosed with FDEIA, it will be critical for him or her to seek guidance from an allergist for ongoing

Table 4. Diagnostic Allergy Tests

Type	Subtype	Description	Positive	Pros/Cons
History		Questionnaire, thorough recall of events leading up to anaphylaxis	Multiple episodes of anaphylaxis only after ingestion of a specific food preceding exercise	
Skin (<i>in vivo</i>)	Skin prick test	Commercial extracts or fresh of suspected food items recently ingested	> 3-mm diameter ³⁰	Pro: quick, low cost, simple Con: must withhold antihistamines before test
	Prick by prick	Tests against fresh fruits and vegetables ³⁴	> 3-mm diameter	Pro: quick, low cost, high accuracy, simple Con: limited to fruit and vegetable allergens, must withhold antihistamines before test
<i>In vitro</i> specific IgE assays	Histamine release test	Amount of histamine released measured ³⁰	≥ 0.35 kU/L	Pro: small amount of blood required, no exposure to allergen, more sensitive than RAST Con: Cost, available only for 10 allergens, histamine has a short half-life making it difficult to capture via blood test
	Basophil activation test	Most successful in identifying omega 5-gliadin in WDEIA ¹¹	≥ 0.35 kU/L	Pro: no exposure to allergen, expensive Con: expensive
	RAST	Measures concentration of serum specific IgE ³⁰	≥ 0.35 kU/L	Pro: no exposure to allergen, negative predictive value of food is high Con: expensive, limited allergens can be tested, uses radioactivity
	ImmunoCAP immuno solid-phase allergy chip	Can test for those with multiple allergens, and determines the pattern of reactivity	≥ 0.35 kU/L ³⁰	Pro: no exposure to allergen, can test > 100 allergens in 1 blood sample Con: does not test for unknowns
Challenges	DBPCFEC	Gold standard ³⁰	Anaphylaxis only upon ingestion of culprit food preceding exercise	Pro: confirms diagnosis, most accurate Con: expensive, time-consuming, induces anaphylaxis, cofactors ³⁵

DBPCFEC = double-blind placebo-controlled food exercise challenge; IgE = immunoglobulin E; RAST = radioallergosorbent test; WDEIA = wheat-dependent exercise-induced allergy.

reevaluation, psychological well-being, and exercise tolerance.³⁵

Prevention therapies including high-dose cromolyn may be helpful in patients with FDEIA.³⁵ However, there is conflicting research. Offering 100 mg high-dose cromolyn to children before any meal followed by exertion should be coupled with the understanding that the efficacy has not been proven.³⁵ In addition, other case reports using premedication with H1 antihistamines are not definitive, and the therapy is controversial because of the possibility of masking of early symptoms. Clearly, more research and clinical trials are needed.

THE ROLE OF THE NP

Clinical

When presented with a case of anaphylaxis, providers often do not consider FDEIA.³⁵ It is important that NPs are aware of the clinical manifestations, appropriate clinical diagnosis, and proper management for this condition. Lack of knowledge of FDEIA can lead to inaccurate diagnoses and inappropriate treatment plans. Collecting a detailed history with allergy-specific questions surrounding the episodes such as the presenting symptoms; the timing of the reaction; the route and amount of possible food allergens; prior history of food tolerance, especially without any physical activity; and precipitating factors is essential.³⁶ Although FDEIA is important to diagnose, the initial management of FDEIA and anaphylaxis should be identical in terms of emergency medical attention, but in FDEIA, there should not be unnecessary diet or exercise modifications. Once an anaphylactic patient is stabilized, an NP should refer to an allergist and registered dietician for management.³⁶

Education

The patient and the family need to understand the diagnosis, the signs and symptoms of anaphylaxis, and the appropriate management of anaphylaxis including the self-administration of epinephrine. To help educate the family, the [Figure 1](#) is a low-literacy handout for use with patients and families. To lessen the patient and parents' anxiety, the NP explores and addresses all of the family's concerns.

For patients with FDEIA, a diet plan sensitive to the individual's situation should be mapped out. If there is any recurrence, the patient should follow up postintervention with the allergist. In any event, should a patient accidentally ingest food with a hint of the culprit allergen, it is highly advised for the patient to carry antihistamines, a self-injectable epinephrine pen, and contact information at all times. As a primary care provider, the NP should provide the prescription for a duo epinephrine autoinjector pack, stressing the importance of always having the device on hand and looking at the expiration date. The NP should also have the patient demonstrate how to properly use the epinephrine pen with an epinephrine trainer pen. A personalized emergency plan and medications for every patient along with a medical alert bracelet are crucial for his or her safety.³⁶ Although allergy and immunology specialists generally perform the tests in specialized academic centers, the NP should be able to provide a preview of what the patient can expect for FDEIA diagnostic testing. The NP plays a crucial role in helping spread awareness for FDEIA with peers because it is often misdiagnosed.

Research

NPs should stay updated on new research on FDEIA because future studies will delve deeper into understanding the pathogenesis of FDEIA, which could lead to a more efficient method of diagnosing FDEIA. Although several pathologies have been reported, the etiology behind FDEIA is still unknown. A few temporary preventative FDEIA methods are promising, but randomized controlled trials are needed. Once a clear underlying cause of FDEIA is found and more studies provide additional evidence to its efficacy, researchers may develop further advancements in this rare condition.

DENOUEMENT

Because N.C. loved both shrimp and exercise, N.C. attended an allergy clinic where she completed a DBPCFEC. The result was positive for shrimp-induced FDEIA. She was asymptomatic while playing tennis in the absence of shrimp ingestion and

therefore is able to continue to enjoy both as long as she is careful about the timing of ingestion (of shrimp) and exercise.

CONCLUSION

FDEIA is a rare form of anaphylaxis in which anaphylaxis occurs when some unspecified degree of physical activity is performed after ingestion of a culprit food. Ingestion of the causative allergen and engaging in exercise are both independently tolerated in patients with FDEIA. The pathophysiology of FDEIA is still unknown, and further research will be necessary for future advancements. An individual with FDEIA must avoid the putative food before and 1 hour after any physical exertion and have injectable adrenaline and antihistamines available at all times in case of emergency because FDEIA can be unpredictable and potentially fatal. The NP should be aware of the clinical manifestations and management of FDEIA to provide an accurate and proper care plan for a patient with FDEIA. **JNP**

References

1. Medveczky T. A dangerous exercise lessons from food-dependent anaphylaxis for the physician. *Am J Emerg Med.* 2014;32:1296.e5-1296.e7.
2. Bonini M, Palange P. Anaphylaxis and sport. *Curr Opin Allergy Clin Immunol.* 2014;14:323-327.
3. Wong GK, Huissoon AP, Goddard S, et al. Wheat dependent exercise induced anaphylaxis: is this an appropriate terminology? *J Clin Pathol.* 2010;63:814-817.
4. Maulitz RM, Pratt DS, Schocket AL, et al. Exercise-induced anaphylactic reaction to shellfish. *J Allergy Clin Immunol.* 1979;63:433-434.
5. Kidd JM, Cohen SH, Sosman AJ, et al. Food-dependent exercise-induced anaphylaxis. *J Allergy Clin Immunol.* 1983;71:407-411.
6. Cianferoni A, Muraro A. Food-induced anaphylaxis. *Immunol Allergy Clin North Am.* 2012;32:165-195.
7. Kushimoto H, Aoki T. Masked type I wheat allergy. Relation to exercise-induced anaphylaxis. *Arch Dermatol.* 1985;121:355-360.
8. Kim CW, Figueroa A, Park CH, et al. Combined effects of food and exercise on anaphylaxis. *Nutr Res Pract.* 2013;7:347-351.
9. Thalayasingam M, Allameen NA, Soh JY, et al. Wheat-dependent exercise-induced anaphylaxis: a retrospective case review from a tertiary hospital. *Postgrad Med J.* 2014;90:488-492.
10. Du Toit G. Food-dependent exercise-induced anaphylaxis in childhood. *Pediatr Allergy Immunol.* 2007;18:455-463.
11. Scherf KA, Brockow K, Biedermann T, et al. Wheat-dependent exercise-induced anaphylaxis. *Clin Exp Allergy.* 2016;46:10-20.
12. Flannagan LM, Wolf BC. Sudden death associated with food and exercise. *J Forensic Sci.* 2004;49:543-545.
13. Chong SU, Worm M, Zuberbier T. Role of adverse reactions to food in urticaria and exercise-induced anaphylaxis. *Int Arch Allergy Immunol.* 2002;129:19-26.
14. Castells MC, Horan RF, Sheffer AL. Exercise-induced anaphylaxis. *Curr Allergy Asthma Rep.* 2003;3:15-21.
15. Robson-Ansley P, Toit GD. Pathophysiology, diagnosis and management of exercise-induced anaphylaxis. *Curr Opin Allergy Clin Immunol.* 2010;10:312-317.
16. Morita E, Kunie K, Matsuo H. Food-dependent exercise-induced anaphylaxis. *J Dermatol Sci.* 2007;47:109-117.
17. Fujii H, Kambe N, Fujisawa A, et al. Food-dependent exercise-induced anaphylaxis induced by low dose aspirin therapy. *Allergol Int.* 2008;57:97-98.
18. Barg W, Medrala W, Wolanczyk-Medrala A. Exercise-induced anaphylaxis: an update on diagnosis and treatment. *Curr Allergy Asthma Rep.* 2011;11:45-51.
19. Jo EJ, Yang MS, Kim YJ, et al. Food-dependent exercise-induced anaphylaxis occurred only in a warm but not in a cold environment. *Asia Pac Allergy.* 2012;2:161-164.
20. Tanaka S. An epidemiological survey on food-dependent exercise-induced anaphylaxis in kindergartners, schoolchildren and junior high school students. *Asia Pac J Public Health.* 1994;1:26-30.
21. Gonzalez-Quintela A, Vidal C, Gude F. Alcohol, IgE and allergy. *Addict Biol.* 2004;9:195-204.
22. Bito T, Kanda E, Tanaka M, et al. Cows milk-dependent exercise-induced anaphylaxis under the condition of a premenstrual or ovulatory phase following skin sensitization. *Allergol Int.* 2008;57:437-439.
23. Del Giacco SR, Carlsen KH, Du Toit G. Allergy and sports in children. *Pediatr Allergy Immunol.* 2012;23:11-20.
24. Ring J, Behrendt H, de Weck A. History and classification of anaphylaxis. *Chem Immunol Allergy.* 2010;95:1-11.
25. Matsuo H, Morimoto K, Akaki T, et al. Exercise and aspirin increase levels of circulating gliadin peptides in patients with wheat-dependent exercise-induced anaphylaxis. *Clin Exp Allergy.* 2005;35:461-466.
26. Palosuo K, Varjonen E, Kekki OM, et al. Wheat omega-5 gliadin is a major allergen in children with immediate allergy to ingested wheat. *J Allergy Clin Immunol.* 2001;108:634-638.
27. Cooper DM, Radom-Aizik S, Schwindt C, Zaldivar F Jr. Dangerous exercise: lessons learned from dysregulated inflammatory responses to physical activity. *J Appl Physiol (1985).* 2007;103:700-709.
28. Tewari A, Du Toit G, Lack G. The difficulties of diagnosing food-dependent exercise-induced anaphylaxis in childhood — a case study and review. *Pediatr Allergy Immunol.* 2006;17:157-160.
29. Aihara Y, Takahashi Y, Kotoyori T, et al. Frequency of food-dependent, exercise-induced anaphylaxis in Japanese junior-high-school students. *J Allergy Clin Immunol.* 2001;108:1035-1039.
30. Asaumi T, Yanagida N, Sato S, et al. Provocation tests for the diagnosis of food-dependent exercise-induced anaphylaxis. *Pediatr Allergy Immunol.* 2016;27:44-49.
31. Simons FE, Arduzzo LR, Bilo MB, et al. International consensus on (ICON) anaphylaxis. *World Allergy Organ J.* 2014;7:9.
32. Fiocchi A, Mirri GP, Santini I, et al. Exercise-induced anaphylaxis after food contaminant ingestion in double-blinded, placebo-controlled, food-exercise challenge. *J Allergy Clin Immunol.* 1997;100:424-425.
33. Sampson HA, Gerth van Wijk R, Bindslev-Jensen C, et al. Standardizing double-blind, placebo-controlled oral food challenges: American Academy of Allergy, Asthma & Immunology-European Academy of Allergy and Clinical Immunology PRACTALL consensus report. *J Allergy Clin Immunol.* 2012;130:1260-1274.
34. Povesi Dascola C, Caffarelli C. Exercise-induced anaphylaxis: a clinical view. *Ital J Pediatr.* 2012;38:43.
35. Feldweg A. Exercise-induced anaphylaxis. *Immunol Allergy Clin North Am.* 2015;35:261-275.
36. Moore L, Kemp A, Kemp S. Recognition, treatment and prevention of anaphylaxis. *Immunol Allergy Clin North Am.* 2015;35:363-374.

Acknowledgments

The authors thank Dr. Sabrina Opiola of Columbia University's School of Nursing for her assistance.

1555-4155/17/\$ see front matter
© 2017 Elsevier Inc. All rights reserved.
<http://dx.doi.org/10.1016/j.nurpra.2017.01.006>