

Exercise-induced anaphylaxis related to specific foods

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We describe the case, documented by challenge results, of a 16-year-old girl with exercise-induced anaphylaxis associated with eating pizza and a cheese sandwich. Patients in whom a specific coprecipitating food has been identified should avoid it for at least 12 hours before exercise. All patients should be instructed to avoid eating 6 to 8 hours before exercise, discontinue exercise at the first sign of symptoms, and exercise only with a companion prepared to administer epinephrine. (J PEDIATR 1995;127:587-9)

The first reported case of exercise-induced anaphylaxis was in a competitive runner who had facial flushing, giant hives, and laryngeal edema whenever he exercised after having eaten shellfish.¹ Neither exercise nor shellfish alone resulted in symptoms. The interval between eating shellfish and symptomatic exercise ranged from 5 to 24 hours. Results of skin tests to shellfish were positive. Sixteen cases were reported the following year.² Most of the patients exercised daily but had symptoms only rarely. Clinical manifestations consisted of generalized pruritus and giant hives progressing variably to angioedema, hypotension, upper airway obstruction, gastrointestinal distress, or wheezing. Half of the patients had a history of allergy and all reported a family history of atopy.²

CASE REPORT

A 16-year-old girl was referred for further evaluation of symptoms that dated back 5 years. While playing basketball she had generalized pruritus and flushing that resolved after administration of diphenhydramine. She had many recurrences, characterized by initial pruritus and flushing, variably followed by giant hives of the arms and trunk, periorbital edema, angioedema of the face and lips, and laryngeal stridor. All attacks followed activities such as running, walking, and, on one occasion, loading the dishwasher. She

competed in high school track as a distance runner, and avoided attacks by not eating before running. Symptoms occurred within 4 hours of eating grains, broccoli, cabbage, cauliflower, eggs, or sandwiches that contained cheese, but never in the absence of exertion. Reactions were more frequent and severe during and preceding menstrual periods.

Shortly before referral the patient participated in a regional pageant. On the day of the contest she took three doses of propranolol to help control anxiety. After the competition, she ate pizza and went swimming. Immediately afterward she had systemic collapse with hypotension, abdominal pain, and diarrhea, and required admission to an intensive care unit.

Medical history was notable for mild asthma and seasonal allergic rhinitis; her medications consisted of injectable epinephrine and inhaled albuterol. There was a family history of atopy, and her brother had mild asthma, allergic rhinitis, and urticaria. There was no family history of anaphylaxis. Physical examination findings were unremarkable.

Pulmonary function and chest radiographs were normal. Skin tests showed a positive reaction to trees, weeds, grasses, dust mite, corn, wheat, rice, peas, peanut, soybean, tomato, cabbage, broccoli, cauliflower, and chocolate. Double-blind food challenges were performed to wheat, rice, tomato, and corn. Only corn was associated with minimal lip swelling. Open challenges to broccoli, cauliflower, cabbage, egg, pizza, and a cheese sandwich all had negative results.

Each food challenge was followed 30 minutes later by a treadmill exercise challenge using the standard Bruce protocol.³ All food-and-exercise challenges were well tolerated except for those including pizza or a cheese sandwich. Pizza gave rise to subjective symptoms of facial and abdominal discomfort, resulting in premature cessation of the test. The challenge to a cheese sandwich resulted in generalized hives, periorbital edema, nausea, emesis, and chest pain with ischemic electrocardiographic changes (Figure) and hypotension within 4 minutes. Symptoms abated and the electro-

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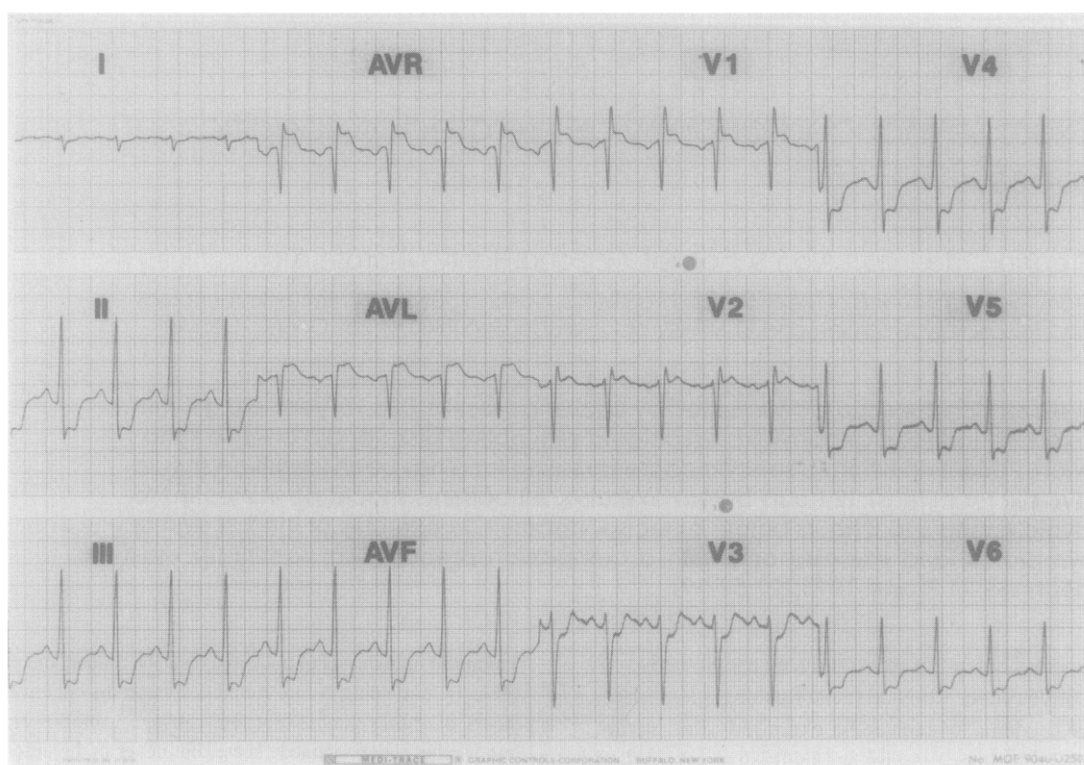


Figure. Electrocardiogram obtained during episode of chest pain 4 minutes after cessation of exercise. Note 3 to 4 mm ST segment depression in leads II, III, AVF, AVL, and V₆, suggesting inferolateral ischemia.

Table. Exercise-induced physical urticarias

	Exercise-induced anaphylaxis	Cholinergic urticaria
Size of wheal	Large (5 to 15 mm)	Punctate
Symptoms with exercise	+	+
Symptoms with passive heat exposure	-	+
Systemic collapse	+	Only in extreme cases
Symptoms reliably reproduced	-	+
Symptoms associated with pulmonary function abnormalities	-	Sometimes
Symptom threshold altered by regular exercise	-	+

cardiogram became normal 30 minutes after the patient received epinephrine subcutaneously, fluids, and diphenhydramine intravenously.

DISCUSSION

The differential diagnosis of exercise-induced anaphylaxis includes cholinergic urticaria, exercise-induced asthma, vocal cord dysfunction, and idiopathic anaphylaxis. The diagnosis of exercise-induced anaphylaxis is made by history and may be confirmed by exercise challenge. This condition can be distinguished by elevation of serum histamine, although this finding has also been shown in cholinergic urticaria.⁴ Positive skin-test reactions to foods that may be co-precipitating factors in exercise-induced anaphylaxis are very sensitive but not specific. Reactivity to aeroallergens does not contribute to the diagnosis. The presence of hives after exertion is characteristic of both exercise-induced anaphylaxis and cholinergic urticaria. Generally the appearance of the hives is distinct in the two conditions (Table). Challenge studies have demonstrated that patients with exercise-induced anaphylaxis have "giant" hives (>5 mm in diameter).⁵ Passive warming experiments have demonstrated that

exogenous heat elicits punctate hives, characteristic of cholinergic urticaria.⁶ Exacerbation of cholinergic urticaria may be associated with airway obstruction⁷ but rarely results in systemic collapse. However, two separate reports have challenged the distinction between exercise-induced anaphylaxis and cholinergic urticaria by performing exercise challenges on patients with a history of exercise-induced systemic collapse.^{8,9} The patients had both punctate hives, associated with cholinergic urticaria, and hypotension, characteristic of exercise-induced anaphylaxis.

The prevalence of exercise-induced anaphylaxis is unknown. The majority of reports describe trained athletes, but it is not clear whether the magnitude and frequency of exercise are independent risk factors. The gender distribution is equal. A family history of exercise-induced anaphylaxis is uncommon. At least half of the patients are atopic, and although some of them have symptoms only after ingesting specific foods, a definite coprecipitating factor can be identified only infrequently. The offending foods—wheat, shellfish, celery, eggs, peaches, and grapes—generally produce positive skin test reactions, but the role of the foods in causing these reactions must be confirmed by challenge.¹⁰ One report described symptoms attributed to celery that occurred only when it was ingested *after* exercise.¹¹ Symptoms have been described with exercise after the ingestion of any food.¹⁰ The patients, two of whom were atopic, did not have skin-test reactivity to foods.

Orally administered sodium cromolyn and sodium bicarbonate have been tried prophylactically, but their efficacy remains unproved.¹⁰ Although studies to support prophylaxis with oral administration of antihistamines are lacking, empiric use is reasonable. Avoiding exertion is not practical, given the sporadic nature of symptoms and the importance that many patients place on exercise. Subcutaneous administration of epinephrine remains the only effective treatment; patients with exercise-induced anaphylaxis should always carry an injection kit. In addition, they should avoid all food 6 to 8 hours before exercise, and those patients for whom a specific food trigger is identified should avoid that food for at least 12 hours. Patients should discontinue exercise at the first sign of symptoms, and exercise only with a friend prepared to administer epinephrine.

Although the pathogenesis of exercise-induced anaphylaxis is poorly understood, biopsy studies have demonstrated mast cell degranulation after exertion.¹² Skin tests with codeine and compound 48/80 (a nonspecific stimulant of connective tissue mast cell degranulation), but not histamine, produce larger wheals after exercise.¹⁰ This suggests that mast cell "sensitization" takes place. Patients with exercise-induced anaphylaxis who have specific foods as coprecipitating factors invariably have positive skin test reactions to

those foods;¹⁰ thus specific IgE mast cell sensitization may also occur. The nature of the contribution of exercise to symptoms is unknown. β -Adrenergic blocking agents, although not previously reported to exacerbate exercise-induced anaphylaxis symptoms, increase both the risk and severity of anaphylaxis, in part because of increased mast cell mediator synthesis and release.¹³

The patient in this case report has several features characteristic of exercise-induced anaphylaxis. Her symptoms are sporadic, are potentially life threatening, and can be avoided by fasting before exercise. Despite the classic history, her case was initially viewed as factitious, given the many negative challenge results. Pediatricians without the facilities to conduct extensive challenge testing should regard similar accounts among their patients with concern and should instruct them in the appropriate precautions.

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