

Cow's milk-dependent, exercise-induced anaphylaxis: Case report of a patient with previous allergy to cow's milk

To the Editor:

In the past decade there has been an increasing number of reports of food anaphylaxis associated with exercise. To date, 2 forms of this clinical entity have been described: reactions following the ingestion of specific foods and reactions following the ingestion of any food.

We describe the case of a 16-year-old girl who had been developing several episodes of anaphylaxis since she was 14 years old. Thirty minutes after the intake of a food that contained cow's milk (cow's milk pudding, cheese sandwich, or rice with milk), symptoms would appear while she was jogging or playing basketball. However, all of these foods were tolerated when their ingestion was not followed by exercise.

The girl had been diagnosed as having allergy IgE-mediated to cow's milk protein at 4 months of age by (a) positive skin prick test results with whole cow's milk extract 5% w/v (Abelló, Madrid, Spain) and isolated cow's milk proteins (10 mg/mL), α -lactalbumin, β -lactoglobulin, and casein (Sigma Chemical, St Louis, Mo) in PBS, (b) specific IgE to the same allergens (RAST Pharmacia, Uppsala, Sweden), and (c) a positive challenge test result with cow's milk. Using a soy formula substitute, she followed a diet that was free of cow's milk. Follow-up visits took place yearly at our outpatient allergy clinic.

At 14 years of age it was proved that she tolerated cow's milk. At that time, the patient still presented sensitivity to milk, though the specific IgE levels were decreasing in the follow-up. (Specific IgE was determined initially by RAST and from 7 years of age onward by CAP Pharmacia) (Table I). From then on the patient tolerated cow's milk; however, she started to show the

TABLE I. Specific IgE antibodies to cow's milk protein at follow-up

Allergen	Antibodies (KU/L)			
	7 y	9 y	14 y	16 y
Milk	16.5	14.4	6.56	4.5
α -lactalbumin	2.6	2.71	4.08	2.7
β -lactoglobulin	1.1	1.06	1.32	1.5
Casein	9.4	7.94	7.62	4.0

anaphylactic episodes mentioned above. She also had a history of pollinosis from the age of 5 years onward.

In the present study, the result of a skin prick test with cow's milk proteins was still positive. Skin prick tests with a battery of food allergens were carried out; these were negative for egg white, wheat flour, shrimp, peanut, hazelnut, apple, celery, and soy and also negative for inhalant extracts, with the exception of grass pollen. Total serum IgE was 23 KU/L. Specific IgE to milk was 4.5 KU/L (Table I).

Another open challenge test with cow's milk was performed; there were no symptoms of any sort. The patient was tested for exercise challenge on a treadmill for 10 minutes; no reaction was elicited. She was also given a challenge test of 15 minutes of outdoor jogging in the hospital garden (adjacent to the emergency room) 30 minutes after an intake of soy milk pudding; this did not produce a reaction either.

When another challenge under the same conditions was carried out, this time with cow's milk pudding, the patient presented immediate-type reactions after 12 minutes of jogging. Itching of the skin was followed by generalized urticaria with swelling of the lips and eyelids, pruritus, and conjunctival injection, pruritus of the throat, dysphagia, dyspnea, and faintness. The patient was immediately treated with epinephrine by subcutaneous injection, with antihistamines and corticosteroids by intravenous infusion, and with salbutamol. This treatment relieved the symptoms within 2 hours.

Since the first such report in 1979,¹ numerous foods have been implicated in food-dependent, exercise-induced anaphylaxis (FDEIAN).^{2,3} There are rare references to milk as a food trigger of FDEIAN. In a study reported by Shadick et al,⁴ milk was found to be a food trigger in 4% of 279 subjects with FDEIAN. This survey was implemented through use of a questionnaire.

To our knowledge, the case we describe is the first written report of FDEIAN in which a symptomatic IgE-mediated allergy is shown to evolve into an asymptomatic sensitivity which at that moment develops into FDEIAN. We think it possible, eventually, that when the sensitivity disappears, the FDEIAN will also disappear.

In FDEIAN, slight sensitivity to the offending food is usually found,² but this is tolerated if the intake is not followed by exercise. Asymptomatic sensitivity is common in the natural history of food allergy, and it could favor

the appearance of FDEIA, as happened with our patient. However, it is remarkable that until now no other cases with a similar profile have been described.

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A prospective evaluation of the adequacy of peak inspiratory flow rates and validation of the Turbutester score in asthmatic individuals with "low" peak expiratory flow rates: Implications for dry powder inhalers

To the Editor:

The negative impact of chlorofluorocarbons on the ozone layer has resulted in the development of novel dry powder inhalers (DPIs). The peak inspiratory flow rate (PIFR) has a direct influence on the amount of drug that is delivered to the lungs via these DPIs. Depending on its design, a propellant-free DPI requires a PIFR of -15 to -60 L/min for optimal drug deposition.

Borgstrom et al¹ studied the deposition of budesonide via the Pulmicort Turbuhaler (AstraZeneca Pharmaceuticals LP). At a PIFR of -60 L/min, 27.7% of the drug was deposited; this compared with 14.8% at -35 L/min. In a study of 101 adult patients with asthma,² the mean PIFR through a Turbuhaler was -59 L/min (range, -26 to -103 L/min). Four patients had PIFRs below 30 L/min. In a study of children <6 years of age,³ 15 of 57 subjects were unable to generate a PIFR <-30 , whereas all children ≥ 6 years of age successfully generated adequate PIFRs.

The possibility that asthmatic individuals with chronic severe airway obstruction or younger patients with low flows were not able to generate adequate PIFRs led us to prospectively examine flows in these patients, both quantitatively—by using an inspiratory flow meter—and qualitatively—via the generation of a Turbutester score.

The Turbutester is an instructional tool designed to help patients learn to use the Turbuhaler optimally. The Turbutester produces a whistle sound when the patient inhales

TABLE I. Baseline characteristics

Characteristic	Total n = 30
Age	
Mean (y)	58.2
Range (y)	8-90
8-10 y (n)	4
40-49 y (n)	3
50-59 y (n)	4
60-69 y (n)	9
70-79 y (n)	6
80-89 y (n)	4
Percent male	32.0
No. of asthma medications	
Mean	2.9
Range	1-7
No. of patients on daily or alternate day prednisone	7
No. of patients receiving prednisone bursts over the past year	9
Inhaled corticosteroid dosage: mean $\pm$ SD (μ g)	625 $\pm$ 378

deeply and forcefully, and the device is standardized ex vivo to produce this sound at a PIFR of <-45 L/min.

This was a prospective study carried out in a group allergy practice. All patients with the diagnosis of asthma who presented for initial or follow-up visits were screened for this study. Peak expiratory flow testing is routinely performed at these visits. A patient was eligible if he or she (1) had stable asthma with a "low" peak expiratory flow rate (PEFR) (<260 L/min), (2) used asthma medication (of any kind) on an as-needed or regular basis, and (3) was capable of performing reproducible and technically adequate PEFR. Current and previous smokers were not excluded, and informed consent was obtained from every participant.

Spirometry was performed with a Burdick flow sensor; recordings obtained within the past 12 months were not repeated. Patients performed 3 PEFR measurements sequentially via a Mini-Wright peak flow meter. Patients were then coached on the use of the Turbutester, and the quality of each patient's efforts was assessed in triplicate, the best effort being recorded.

Turbutester measurements were scored according to the following scale: 0, no sound; 1, sound lasting <1 second; 2, sound lasting 1 to 2 seconds; 3, sound lasting >2 seconds.

To avoid investigator bias, the peak inspiratory flow was recorded in triplicate through use of the In-Check device (an inspiratory peak flow meter) only after the Turbutester score was assigned.

Thirty patients were eligible for this study (Table I). The population included 26 adults and 4 children (age range, 8 to 90 years). The baseline FEV₁ ranged from 17% to 105% of predicted normal. Seventy-three percent of the patients were atopic. Five patients had histories of smoking; 4 were current smokers. Nearly all patients (27 of 30) were currently on a regimen of high-potency inhaled corticosteroids (fluticasone propionate or budesonide).