
Occupational allergic rhinoconjunctivitis and asthma due to fennel seed

Howard J Schwartz, MD*; Richard T Jones†; Amelia R Rojas, MD‡; Diane L Squillace§; and John W Yunginger, MD||

Background: A patient with complaints of rhinitis and asthma occurring at work presented for consultation.

Objectives: To evaluate the role of the foods and spices with which he worked, in the causation of his complaints, and to evaluate his immune reactivity to these materials.

Methods: Allergy skin testing and in vitro RAST assays were carried out. After demonstrating specific reactivity to fennel, SDS-PAGE electrophoreses was carried out.

Results: Positive skin tests to grass, ragweed, and freshly prepared fennel seed were found. Serum IgE antibodies to fennel were quite high. Immunoblotting studies showed reactions to two components in fennel extract as well as to components in mugwort, paprika, short ragweed, and black pepper.

Conclusion: This case of occupational rhinitis and asthma in an atopic individual involves sensitivity to unique allergens in fennel, with molecular weights of 67 to 75 KD.

Ann Allergy Asthma Immunol 1997;78:37–40.

INTRODUCTION

There has been a growing awareness of the role of IgE-mediated allergic reactions to foods causing rhinitis, asthma, anaphylaxis, and even death in adult patients.^{1,2} There have been several cases describing significant reactions to spices as well^{3–7} although these reactions are more difficult to document. Van Toorenenbergen et al have raised

the issue of IgE-anti-spice as a cause of hives, angioedema, and urticaria in a series of patients suspected of having ingestant food allergy.⁶ In addition, there have been several case reports of occupational allergic airways disease in workers handling spices.^{3,4,7} We report a case of clear-cut allergic rhinitis and asthma due to the inhalation of fennel seed dust in a sausage maker.

CASE REPORT

A 27-year-old Caucasian male native Ohioan was seen in consultation with a 1-year history of symptoms of allergic rhinitis and a 3-week history of trouble breathing at work, with cough, chest congestion, and possible wheeziness. These symptoms would especially occur when the patient would add spice to the sausage being made at a sausage manufacturing plant where he had been employed for several years. There was no previous history of allergic disease, sinusitis, pneumonia, or asthma. There was ½ pack per day cigarette smoking for 5 years and no history of food or drug allergy. He did

not eat sausage from work. In the making of sausage the patient worked with pork, beef, salt, pepper, garlic, paprika, fennel seed, and hog casings. He lived in a home without exposure to pets or feathers.

The patient worked from 6 AM to 4 PM. Monday mornings were symptom-free, but he became progressively worse throughout the work week and was “miserable” by Friday or Saturday. The patient felt less ill, and on Sunday he would feel “normal.” The patient did note that his symptoms would flare at about 7 PM at night, but he had no late night symptoms.

He worked in a 20 foot by 30 foot room, in which windows were closed. There was an overhead gas heat hot air blower, with no vents for exhaust or air return. Air conditioning was rarely used. A typical work day involved major exposure to fennel between 6 AM and 10 AM, during which he seasoned 2,000 pounds of sausage with 20 pounds of fennel seed over several hours. Ground fennel seed was worse than intact seed. The patient would develop sneezing, runny nose, and local itching if ground fennel “got into” an open cut or “sore” on his hands.

He sometimes experienced sneezing, nasal congestion, and a sense of being unwell if he ate certain Italian foods with sauces (which presumably contain fennel). He can eat garlic without trouble, but garlic powder can sometimes cause sneezing. He eats celery in small amounts, without clinical difficulty.

Since being seen, he has developed clinical seasonal allergic rhinitis, but his experiences with occupational difficulty were not in pollen season.

Physical examination revealed a

* Airways Disease Center, Department of Medicine, University Hospitals of Cleveland, Case Western Reserve University and University Suburban Health Center, Cleveland Ohio.

† Allergic Diseases Research Laboratory, Mayo Clinic and Foundation, Rochester, Minnesota.

‡ Mayo Graduate School of Medicine, Rochester, Minnesota; Present address: Beloit Clinic, Beloit, Wisconsin.

§ Allergic Diseases Research Laboratory, Mayo Clinic and Foundation, Rochester Minnesota.

|| Department of Pediatric and Adolescent Medicine and Department of Medicine (Allergy), Mayo Clinic and Foundation, Rochester Minnesota.

Received for publication March 1, 1996.

Accepted for publication in revised form July 24, 1996.

well developed, well nourished young man with a cough, reddened conjunctival membranes, boggy nasal mucus membranes, and scattered expiratory wheezes on examination of the chest. Laboratory studies revealed reductions in the first second expiratory volume and mid-expiratory flow rates which improved after aerosol bronchodilator therapy (Table 1). Allergy skin testing by the prick method revealed significant reactions to grass and ragweed pollen, and several fungi. Prick testing to freshly prepared fennel seed extract was strongly positive, with all other relevant prick tests to foods being negative, especially to beef, pork, garlic, and paprika. Prick skin test to birch tree pollen was negative. The patient refused any blinded challenge studies or work simulation studies in the laboratory.

MATERIALS AND METHODS

In the Allergic Disease Research Laboratory, Mayo Clinic, serum IgE antibodies were measured to birch pollen, apple, celery, and mugwort pollen using standard reagents (Table 2). In addition, fresh extracts of several spices supplied by the patient were used to prepare "custom" solid-phase immunoassay reagents. The patient's serum was tested for IgE antibodies to garlic, black pepper, paprika, red pepper, ground fennel, and freshly ground fennel seed.

Polyacrylamide electrophoresis in 12% gels containing 1% sodium dodecyl sulfate (SDS-PAGE) was carried out with a variety of extracts, including fennel, birch pollen, black pepper, pa-

prika, short ragweed pollen, *D. farinae* mite, garlic, and mugwort pollen. Gels were either stained for protein with Coomassie blue or were blotted onto nitrocellulose membranes, which were subsequently blocked with non-fat milk, probed with the patient's serum, washed, reacted with ¹²⁵I-labeled anti-human IgE, washed again, and exposed to x-ray film to prepare autoradiographs.

Inhibition immunoassays were performed as follows. An in-house extract of fennel seeds was prepared by grinding the seeds using a mortar and pestle, after which the seeds were extracted 1:10 wt/vol in phosphate-buffered saline by mixing overnight at 4 °C. The extract was recovered by centrifugation and coupled to cyanogen bromide-activated microcrystalline cellulose particles to prepare a solid-phase allergen. For inhibition immunoassay experiments, to explore the possible cross-allergenicity of fennel with other sausage ingredients or pollens, the patient's serum was preincubated with varying quantities of either fennel extract or extracts of garlic, mugwort pollen, or birch pollen, then mixed with the solid-phase fennel allergen. After washing steps, the solid-phase allergen was next mixed with radiolabeled anti-IgE, incubated and washed as before, and then counted in an automatic gamma spectrometer.

RESULTS

By immunoassay, the patient's serum did not contain elevated IgE antibodies to birch pollen, whereas IgE antibodies to mugwort pollen and garlic were

Table 2. Specific IgE in Patient's Serum

	IgE Antibody (% negative control)
Standard inhalant and food allergens	
Apple	271%
Celery	1477%
Birch	433%
Mugwort	558%
Custom food reagents	
Ground fennel	2769%
Fennel seed	2245%
Garlic	579%
Black pepper	313%
Red pepper	277%
Paprika	336%

Results are expressed in terms of percent negative control: negative ≤150%, borderline = 150% to 450%, and positive ≥450%.

mildly elevated (Table 2). IgE antibodies to fennel seed were quite elevated. These in vitro tests largely confirmed results of in vivo skin tests. The Coomassie-stained SDS-PAGE gel showed unique banding patterns of varying intensity with each extract. The SDS-PAGE experiments were done in the presence of dithiothreitol, a reducing agent; therefore, the high molecular weight bands seen with fennel do not represent aggregates (Fig 1). The immunoblotting studies showed that our patient reacted to two components in fennel extract, as well as to components in mugwort pollen, paprika, short ragweed pollen, and black pepper. The fennel allergens appeared to be unique with apparent molecular weights of 65 to 75kD. These test bands were not seen with the other allergens tested.

Inhibition immunoassays gave the following results. Addition of varying quantities of fennel extract produced a dose-dependent inhibition of binding of IgE antibodies to the solid-phase fennel allergen, whereas addition of more concentrated extracts of garlic, mugwort pollen, and birch pollen produced insignificant (<15%) inhibition. We concluded that neither garlic, mugwort pollen, or birch pollen contained

Table 1. Pulmonary Function at First Visit

	Predicted	Before Treatment	After Treatment
* FVC (L)	5.15	4.48	4.67
† FEV ₁ (L)	3.78	2.87	3.27
‡ FEF _{25-75%}	4.49	1.36	2.06

* FVC Forced vital capacity, L.

† FEV₁ First second forced expiratory volume, L.

‡ FEF_{25-75%} Forced expiratory flow rate, from 25% to 75% of the total effort in L/sec.



Figure 1. Coomassie blue-stained 12% SDS-PAGE gel. Molecular weight marker proteins are at both ends of the gel (bands 1 and 10). Band 2 is mugwort; band 3, garlic; band 4, *D. farinae*; band 5, short ragweed; band 6, paprika; band 7, black pepper; band 8, birch; and band 9, fennel.

allergens that were cross-reactive with fennel (Table 3).

DISCUSSION

Fennel is a popular herb, known since ancient times and widely used both as a flavoring and as a scent. Photodermatitis and contact dermatitis have been described in some individuals. Allergic reactions have been reported following its ingestion.

Seuri et al have described two cases of occupational asthma and rhinitis caused by occupational exposure to garlic in sausage makers,⁷ and a few other cases of occupational garlic allergy have been described.^{3,4} Two of these cases were in otherwise atopic people. Our patient, a young man with an atopic predisposition, represents the first case of occupational rhinitis and asthma from inhaling fennel seed. The evidence for this is historical and is

supported by both in vivo and in vitro evidence of specific anti-fennel IgE antibodies. He refused a work simulation exposure in the laboratory, and of interest, does not eat sausages, so possible reactions to ingested fennel could not easily be assessed.

This patient also shows evidence of prick test reactivity to a variety of grass and ragweed pollens; but negative in vivo and in vitro reactions to tree pollen, particularly birch. The immunoassay for IgE antibody to mugwort was weakly positive. This is of some interest, since there are reports from Europe of sensitivity to several foods in patients also allergic to birch and mugwort pollens.

While at the present time we have no direct immunochemical evidence, the lack of birch pollen test reactivity and the absence of exposure to mugwort suggests that this patient's fennel

Table 3. Inhibition immunoassays

Inhibitor Added	Dilution	% Inhibition
None	—	0%
Fennel	1/27	84%
	1/81	74%
	1/243	53%
	1/729	32%
	1/2187	13%
Garlic	Neat	7%
	1/3	7%
	1/9	6%
	1/27	4%
	Neat	10%
Mugwort	1/3	4%
	1/9	6%
	1/27	5%
	Neat	11%
	1/3	12%
Birch	1/9	5%
	1/27	5%

seed inhalant allergy is not due to shared epitopes with other inhalant allergens. The issue of inhalant allergic disease to occupationally encountered foods is an issue deserving further study in the exposed worker population.

REFERENCES

1. Yunginger JW, Sweeney KG, Sturner WQ, et al. Fatal food-induced anaphylaxis. *JAMA* 1988;260:1450–2.
2. Yunginger JW, Nelson DR, Squillace DL, et al. Laboratory investigation of deaths due to anaphylaxis. *J Forensic Sci* 1991;36:857–65.
3. Lybarger JA, Gallagher JS, Pulver DW, et al. Occupational asthma induced by inhalation and ingestion of garlic. *J Allergy Clin Immunol* 1982; 69:448–54.
4. Falleroni AE, Zeiss CR, Levitz D. Occupational asthma secondary to inhalation of garlic dust. *J Allergy Clin Immunol* 1981;68:156–60.
5. Van Toorenbergen AW, Dieges PH. Immunoglobulin E antibodies against coriander and other spices. *J Allergy Clin Immunol* 1985;76:477–81.

-
6. Van Toorenbergen AW, Dieges PH. Demonstration of spice-specific IgE in patients with suspected food allergies. *J Allergy Clin Immunol* 1987;79:108-13.
7. Seuri M, Taivanen A, Ruoppi P, et al. Three cases of occupational asthma and rhinitis caused by garlic. *Clin Exp Allergy* 1993;23:1011-4.
8. Yunginger JW, Adolphson CR. Standardization of allergens. In: Rose NR, de Macario EC, Fahey JL, et al, eds. *Manual of clinical laboratory immunology*, 4th ed. Washington DC: American Society for Microbiology, 1992;678-84.
- Request for reprints should be addressed to:*
Howard J Schwartz, MD
University Suburban Health Center
1611 So Green Rd, Suite 265
Cleveland, OH 44121
-