

Immediate and late onset asthma from occupational exposure to soybean dust

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Summary

Most patients sensitive to soybean experience gastrointestinal symptoms, urticaria, angioedema, and asthma after ingestion. However, we report here a previously non-allergic patient who developed immediate and late onset asthma after breathing soybean flour used in the manufacture of food supplements. She exhibited positive immediate and late skin test sensitivity as well as a positive bronchial challenge to a soybean flour extract. In contrast to another patient with an anaphylactic response after soybean ingestion, the radioallergosorbent test (RAST) to soybean antigen was negative in our patient.

Introduction

Soybean products are widely used throughout the food industry and anaphylactic reactions to soybean are well appreciated (Cook, 1960; Mortimer, 1961; Mendoza, Meyers & Snyder, 1970). However, the development of allergic asthma from industrial exposure to the processing of soybeans has not been emphasized. In 1934, Duke described five patients who experienced asthma while working in a soybean mill. There are also a few other reports of asthma resulting from occupational exposure to soybean dust in the available literature (Olsen & Prickman, 1936; Wrightman, 1938; Peters, 1965). We have recently had the opportunity to study the pulmonary and immunological responses of a patient who experienced both immediate and late onset asthma after occupational exposure to soybean flour. While our patient exhibited both immediate and late skin test sensitivity in addition to a positive bronchial challenge, specific IgE was not detectable to the soybean antigen by the radioallergosorbent test (RAST). In another patient who experienced anaphylactic symptoms after ingestion of soybean material, the RAST was strongly positive. This difference may mean that different antigens are responsible for the respective clinical manifestations.

Case history

E.F. is a 27-year-old executive secretary of a dairy food product company which uses soybean flour in its manufacturing process. She has no prior history of hay fever or

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asthma, and she eats cooked soybean products without difficulty. Four years after beginning her present employment, she first experienced coughing, wheezing, dyspnoea, sneezing, and lacrimation of 30–60 min duration which would begin shortly after arriving at work. The symptoms would subside and then recur 5–6 hr later. These episodes occurred only on days when soybean flour was used in the factory.

When seen by us her physical examination, complete blood count, chest X-ray films, and routine spirometry were normal. Intradermal testing to common inhalant antigens was negative.

A diagnosis of asthma due to soybean dust was made, and treatment begun with inhalation of sodium cromoglycate, 20 mg q.i.d. This therapy successfully controlled her symptoms when exposure was low, but it did not prevent asthma with high level exposure. At present, the patient is located in a new office several miles from the factory and has had a complete remission thus far of 6 months.

Materials and methods

As a consequence of the patient's exposure to various soybean flours, casein, lecithin, whey, and skim milk, aqueous extracts of these materials were prepared and serially diluted on a weight-volume basis (Phillips, 1967). After sterilization by Millipore filtration, the antigens were used for intradermal testing. In 15 min, the skin tests were read with a positive response defined as a 6–8 mm weal. In addition to our patient, ten atopic and ten normal subjects were skin tested to the soybean flour extract (atopic individuals are defined as those having a seasonal history of rhinitis or asthma with two or more positive skin tests).

A methacholine inhalation challenge was performed while the patient was asymptomatic (Parker, Bilbo & Reed, 1965). FEV₁ and FVC were recorded on a vitalograph spirometer.

Bronchial challenges to soybean flour and skim milk extracts were performed as recommended by Chai *et al.* (1975) with the following modification: all extracts were administered by a DeVilbiss No. 40 nebulizer powered by a DeVilbiss compressor delivering a flow rate of 11 l/min. The initial broncho-provocation dose was the lowest concentration eliciting a 6–8 mm skin weal with extracts of 1:10⁶ to 1:10² weight-volume basis.

Maximum expiratory flow-volume curves (MEFV) using air and an 80% helium to 20% oxygen mixture, as described by Dosman *et al.* (1975) and modified by Storms, Dick & Busse (1976) were obtained during an asymptomatic period. These results are expressed as maximal expiratory flow rate (MEFR) in l/sec at 50% (V_{max50}) and at 25% (V_{max25}) vital capacity. The percentage increase in flow with the helium-oxygen mixture at 50% (ΔV_{max50}) and 25% (ΔV_{max25}) of vital capacity was calculated by the formula:

$$\frac{\text{flow l/sec He-O}_2 - \text{flow l/sec air}}{\text{flow l/sec Air}} \times 100.$$

Total serum IgE from E.F. was determined by the Pharmacia Phadebas Kit. Serum samples from our patient and a patient with an anaphylactic response after soybean ingestion were tested for specific IgE to soybean by the RAST.

Serum from E.F. was tested for precipitating antibodies to soybean extract by the double-diffusion Ouchterlony technique. A similar method was used to detect antibodies to thermophilic actinomycetes species.

Results

Intradermal skin test reactivity to soybean flour extract was present in our patient at a $1:10^5$ weight-volume dilution. Furthermore, 5 hr afterward there was diffuse erythema, swelling, and warmth involving the entire upper arm. Immediate and late skin test reactivity to casein, lecithin, whey, and skim milk were absent. None of the atopic nor any of the normal subjects exhibited positive responses to the intradermal soybean extract (Table 1).

Table 1. Results of skin survey with soybean flour extract*

Survey population†	No. tested	Positive response‡		
		Soybean flour extract $1:10^5$ w/v	Histamine 0.05 mg/ml	Coca's solution
Patient E.F.	1	1	1	0
Normals	10	0	10	0
Atopics	10	0	10	0

* Intradermal test with 0.02 ml of extract.

† See Methods.

‡ Positive response is a 6–8 mm weal at 15 min.

Table 2. Spirometric results in soybean sensitive patient

	FEV ₁ (ml)	Predicted FEV ₁ (%)	FVC (ml)	Predicted FVC (%)
Predicted normal*	3300	—	3800	—
Methacholine challenge†				
Baseline	3600	109	4500	118
After challenge	1900	58	2950	78
Bronchoprovocation with soybean extract‡				
Baseline	3650	111	4550	120
After challenge	2100	64	2900	76

* Kory *et al.* (1961).

† See Methods.

‡ See Methods.

Five breaths of a 25 mg/ml solution of methacholine produced a 51% fall in predicted FEV₁ 5 min after inhalation consistent with the diagnosis of asthma (Table 2).

Bronchial challenge resulted in a 47% drop in predicted FEV₁ accompanied by coughing and audible wheezing, 10 min after five inhalations of a $1:10^2$ weight-volume solution of the soybean flour extract. There was no significant change from baseline after five inhalations of a $1:10^3$ weight-volume solution of skim milk extract (Table 2).

Analysis of the MEFV curves showed a significant rise in flow rates after breathing He–O₂ at both 50% and 25% of vital capacity (Table 3). These results imply that there was no peripheral airway obstruction between attacks.

Table 3. Results of helium-oxygen studies

	$V_{\max 50}^*$ (l/sec)	$V_{\max 25}$ (l/sec)	$\Delta V_{\max 50}^\dagger$ (%)	$\Delta V_{\max 25}$ (%)
He-O ₂	4.29	2.33	54	61
Air	2.79	1.45	—	—

* $V_{\max}$ is maximal expiratory flow (l/s) at 50% and 25% of vital capacity.

† $\Delta V_{\max}$ is calculated by determining the difference in flow rates breathing both air and an 80% helium-20% oxygen mixture and expressing that difference as a percentage of air flow (see Methods).

Total serum IgE level was 50 iu/ml with the normal adults range 33-915 iu/ml. In patient E.F. a specific IgE to soybean could not be demonstrated using the RAST (E.F. = 120% of control; positive = 200%). In contrast, the patient with an anaphylactic response upon ingestion of soybeans had a positive RAST (3234% of control).

No precipitating antibodies to soy flour extract were demonstrated in the serum of E.F. nor were precipitating antibodies to thermophilic actinomycetes species found.

Discussion

Occupational exposure to organic dust may result in pulmonary hypersensitivity reactions, including asthma, particularly in atopic persons. We could find only one other of the fifty-five employees in the factory described in this study who had any respiratory difficulties. This person resigned because of the dusty conditions. Our limited study does not allow us to draw any conclusion as to the frequency of respiratory symptoms related to occupational soybean dust exposure, nor whether atopic subjects would be at a higher risk of symptoms.

Our findings demonstrate that soybean flour provokes asthma in our patient and that the reaction is probably allergic. The bronchial challenge to soy flour provoked an acute attack of asthma, but this does not exclude the possibility of the reaction being caused by direct bronchial irritation. However, irritation is an unlikely explanation since symptoms occurred with minimal exposure and were not provoked by the bronchial challenge to the skim milk extract.

Our patient's positive intradermal test to a dilute soy flour extract is in keeping with previous reports (Duke, 1934; Olsen & Prickman, 1936; Wrightman, 1938; Peters, 1965). The reaction appears to be specific, in that our study of a group of normals and atopic subjects without significant soybean exposure did not demonstrate positive skin test reactivity. Moreover, our patient did not have any reactivity by skin testing or bronchial challenge to other potential antigens to which she was exposed.

The dual skin test response and history of late onset asthma exhibited by our patient imply an IgE mediated mechanism. In three previously described cases of soybean dust asthma, a positive Práusnitz-Küestner reaction has been demonstrated (Duke, 1934; Wrightman, 1938; Peters, 1965), and late onset asthma followed a positive conjunctival challenge in one patient (Olsen & Prickman, 1936). Solley *et al.* (1976) have recently demonstrated that the late phase of the immediate wheal and flare skin reaction is dependent upon IgE antibodies. The fact that specific IgE antibodies could not be identified by the RAST may be due in part to the low levels of total IgE

(Berg & Johansson, 1974). However, the improvement in asthma following sodium cromoglycate therapy suggests that the mediators of the classical anaphylactic response may be playing a major role in our patient since cromoglycate is known to inhibit their release from sensitized mast cells (Brogdon, Speight & Avery, 1974).

We have cared for a patient whose respiratory symptoms were related to exposure to soybean dust. The development of immediate and late onset asthma from inhalation of organic dusts has been reported by several authors (Busse & Schoenwetter, 1975; Wilbur & Ward, 1976; Hendrick, Davies & Pepys, 1976). It is likely that our patient represents another case of occupational exposure to an antigen capable of inducing *de novo* the development of allergic asthma. Given the large quantities of soybeans used in the food industry, it is highly probable that other persons exposed to this antigen could also develop soybean dust asthma.

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