Tests for sensitisation in occupational medicine practice — the soy bean example

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Objective. To determine the prevalence of sensitisation to soy bean measured by specific IgE and skin prick tests (SPTs) and to examine the association between evidence of sensitisation to soy bean allergens and symptoms of allergic disease.

Design. Cross-sectional study. Questionnaire survey. A venous blood sample was taken for specific IgE testing, and SPTs for common allergens and soy bean dust were performed.

Setting. Soy bean mill.

Participants. A volunteer sample of 22 workers exposed to soy bean dust; the first 20 non-exposed workers presenting to the National Centre for Occupational Health clinic formed the control group.

Main outcome measure. Immunological tests for sensitisation and symptoms of respiratory and allergic disease.

Results. Eight of the exposed workers had positive skin reactions to either full-fat or defatted soy bean. None of the controls was SPT-positive. Eight of the exposed workers had increased levels of soy-specific IgE of whom only 4 were SPT-positive and had an increased level of soy-specific IgE. One of the control workers had an increased level of soy-specific IgE. Workers with an increased specific IgE or SPT positive to soy bean did not have more symptoms than workers with negative tests. However, work-related breathlessness was significantly higher in the exposed group ($P < 0,05$).

Conclusions. The data suggest that the immunological tests for sensitisation were not useful in identifying workers with soy bean-related disease but that tests for sensitisation were linked to exposure.

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Skin prick tests (SPTs) for the diagnosis of platinum salt sensitivity (PSS) demonstrate the potential utility of sensitisation tests in the monitoring of workers exposed to workplace allergens.[1,2] A positive SPT to platinum salts is

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important in the diagnosis of platinum salt sensitivity as it has a high positive predictive value for asthma caused by platinum salts.[3] *In vitro* tests like the radio-allergosorbert test (RAST) for specific IgE have proved less useful.[4] Work at the National Centre for Occupational Health has confirmed these findings: a recent prospective study showed that the SPT had a 100% positive predictability rate for work-related symptoms (A. E. Calverley — unpublished data).

Unfortunately the usefulness of SPTs in PSS has not been realised with regard to other agents such as soy bean. Studies on asthma caused by the inhalation of soy bean dust in Cartagena, Spain, found that at least 90% of patients with asthma had high levels of IgE specific to soy bean components.[5] Of these 87% had a positive SPT for soy bean extract. In contrast to these findings supporting the potential value of SPT and specific IgE in soy bean-exposed individuals, a study found that all 19 workers exposed to soy bean had positive skin reactions but so did 19 of the 20 unexposed control subjects.[6] There was an increase in specific IgE levels in 15,8% of the exposed workers and only 5% of the control group tested. A higher prevalence of chronic respiratory symptoms was found in the soy bean workers, but the difference was statistically significant only for dyspnoea.[6] A study by Goodwin[7] that investigated soya protein-specific IgE antibody levels relative to ingested soya protein found a prevalence of 3,8% in a normal population.

The contrasting findings of these and other studies led to the survey of a small group of workers exposed to soy bean dust reported in this paper. The objectives were to determine the prevalence of sensitisation to soy bean measured by specific IgE and SPT, and to examine the association between evidence of sensitisation to soy bean allergens and symptoms of allergic disease.

Patients and methods

Twenty-two of 41 day-shift soy bean-exposed workers (53%) were studied: 10 were clerical and maintenance workers (low-exposure group) and 12 were millers and packers (high-exposure group). The first 20 workers presenting to the National Centre for Occupational Health clinic who were willing to participate, did not have occupational asthma and were not exposed to soy bean at work formed the control group. Full-fat and defatted soy bean powder (the major products of the study workplace) were obtained from the factory and SPT antigens were extracted in the usual manner[5] with 0,9% NaCl at a 5% (weight/volume) ratio. After being stirred for 1 hour at room temperature, the samples were centrifuged at 22 000 g for 20 minutes and the supernatant dialysed for 24 hours against distilled water. The samples were filtered through a 0,22 µm pore size membrane.

Each participant had SPTs for full-fat and defatted soy bean, a positive and negative control and the standard battery of 8 common allergens: mite, mould mix, dog hair, cat epithelium, Bermuda grass, grass pollen mix, duck feathers and tree mix (Bayer-Miles (Pty) Ltd). Skin reactions were observed by the first author. A reaction was considered positive if a wheal, flare and itch were present — only reactions larger than the negative control were regarded as positive. The positive histamine control was used as a 4 + reading and the rest of the reactions were read in comparison to the positive histamine control.[8] Five millilitres of blood were taken from both the exposed workers and the controls. The blood was spun down and the serum removed and stored at –20°C. A Pharmacia RAST test for soy bean using the Cap system was performed on all the serum samples according to the manufacturer's instructions.

Table I. Sensitisation to soy bean and common allergens, symptoms, smoking status and soya consumption of workers exposed to soy bean dust

Subject	RAST soy bean	SPT soy bean	SPT CA	Symptoms	Smoking status	Soya consumption (portions per week)
1	High	+D	5	E, N	No	1
2	High	+B	5		No	1
3*	High	+F	0		Yes	1
4	Medium	+F	6		No	4
5*	Medium	—	1	C, P, W, B, N	No	12
6	Low	—	0	W, S	No	1
7	Low	—	6	C, W, N	Yes	1
8*	Low	—	0	C, W	Yes	0
9	Absent	—	0	W, B, N	Ex	1
10	Absent	—	1	S	Yes	5
11	Absent	+F	3		No	2
12	Absent	+F	0	B	Yes	1
13	Absent	—	0	B, E	Yes	1
14*	Absent	—	1	C, B, E, N	Yes	1
15*	Absent	—	0	C, P, E	No	1
16*	Absent	—	0	C, P	Yes	21
17*	Absent	+D	0	B	No	0
18*	Absent	—	0	B	No	2
19*	Absent	—	0	C, B, E, N	Ex	4
20*	Absent	—	0	C, P, E, N, S	Yes	1
21*	Absent	—	0	P, E	Yes	1
22*	Absent	+D	0		No	1

SPT = skin prick test; +D = positive SPT, defatted soy bean; +F = positive SPT, fatted soy bean; +B = positive SPT, fatted and defatted; CA = common allergen; C = cough; W = wheeze; P = phlegm; B = breathlessness; E = eye; N = nose; S = skin.
* High-exposure workers.

To determine clinical symptoms, work exposure and work-related symptoms, a modified version of the American Thoracic Society questionnaire[9] on respiratory disease was administered by two trained interviewers.

Asthma was defined as wheeze with tightness of the chest at night or first thing in the morning. Chronic bronchitis was defined as cough and phlegm on most days for 3 consecutive months and at least 2 consecutive years. A symptom was work-related if it occurred at work and improved when on holiday. The workers were also asked about acute symptoms (such as eye, nose and skin irritation) experienced during exposure to dust at work.

Results

It can be seen from Table I that of the 22 exposed workers, 8 were RAST-positive to soy bean; of these 3 had a high score and were SPT-positive to one of the soy bean products. One control subject had a RAST weakly positive to soy bean.

Eight (36%) of the exposed group were SPT-positive for either full-fat or defatted soy bean, with 1 worker positive for both. None of the control group was SPT-positive for the soy bean extracts. Eight of the exposed group (36%) were SPT-positive for one or more common allergens and 4 were positive for both the soy bean extracts and three or more common allergens. Not shown in the table is that 50% of the control group was SPT-positive for one or more common allergens.

Table II shows the prevalence of symptoms in exposed workers and in the control group. Although the prevalence of work-related cough and breathlessness was higher in the exposed group than in the control group, the difference between the groups was not statistically significant ($P > 0,05$).

Table II. Symptoms in soy bean workers and controls

	Soy bean workers ($N = 22$)				Controls ($N = 20$)			
	With symptoms		Work-related		With symptoms		Work-related	
Symptom	No.	%	No.	%	No.	%	No.	%
Cough	8	36	4	18	8	40	1	5
Phlegm	5	22	1	5	8	40	1	5
Wheeze	5	22	0		7	35	0	
Breathlessness	8	36	5	22	11	55	1	5
Cough + phlegm	4	18	1	5	6	30	0	
Asthma	2	9	0		1	5	0	
Chronic bronchitis	1	5	NA		4	20	NA	
Eye	7	32	NA		6	30	NA	
Nose	7	32	NA		4	20	NA	
Skin	3	13	NA		3	15	NA	

NA = not available.

Table III examines the association between tests for sensitisation and symptoms. Within the groups, determined by their RAST response to soy bean, there was no positive relationship between SPT for soy bean and symptoms.

Table III. RAST response to soy bean and SPT for soy bean and symptoms

	RAST response to soy bean			
	RAST-positive ($N = 8$)		RAST-negative ($N = 14$)	
	+SPT soy bean	–SPT soy bean	+SPT soy bean	–SPT soy bean
No.	4	4	4	10
Cough (%)	0	75	0	50
Phlegm (%)	0	25	0	40
Wheeze (%)	0	100	0	10
Breathlessness (%)	0	25	50	60

The capacity of a positive sensitisation test (either RAST- or SPT-positive) to predict disease was assessed by calculating the positive predictive value (PPV) of a positive test for the symptom complex of cough, wheeze or breathlessness. Despite the lax criteria for disease diagnosis (any of three symptoms), the PPV was only 50%, confirming that a positive RAST or SPT was poorly predictive of disease as measured by symptom reporting.

Discussion

The notable findings of this study to investigate sensitisation and symptoms in soy bean-exposed workers and controls, were the poor association between SPT, soy bean-specific IgE and symptoms, and the relatively low prevalence of positive tests of sensitisation (e.g. compared with the 90% found in the Cartagena study[5]).

Possible explanations for our finding are worthy of consideration because they apply, at least in part, to many agents and situations apparently suitable for testing sensitisation to workplace agents.

The study population was small; consequently it is possible that no worker had work-related allergic disease and associations between symptoms and tests for sensitisation would, therefore, not be found. This is particularly important in the context of cross-sectional study designs which investigate a survivor population comprising workers who have tolerated the work environment.

It is nevertheless interesting that about one-third of exposed workers had positive tests unrelated to symptoms. Reasons may include the antigens, the SPT method and the subjects.

The specific soy bean antigens responsible for food allergies are high-molecular-weight proteins ranging from 50 to 60 kilo-daltons (kD)[10] as opposed to the low-molecular-weight protein of 8 kD responsible for respiratory allergies.[5] The specific soy bean antigen used for the RAST in our study was of a high-molecular-weight protein and therefore could not identify workers with soy bean-specific IgE against a low-molecular-weight antigen. The study by Gonzalez *et al.*[5] showed that IgE specific to shell components and to shell-depleted soy bean grains was important.[5] The use of the right antigenic component when preparing SPT extracts is also an important consideration. The asthma patients studied during the Cartagena outbreak had SPTs positive for shell extracts;[5] in our study soy bean powder was used and this may have been a poor antigen.

A study undertaken during asthma outbreaks in Barcelona showed a difference in the proportion of subjects with IgE

specific for commercially prepared soy bean antigens (74,4%) and the soy bean extracts that were prepared from the soy bean dust collected on site (84,9%).[11] This shows that although cross-reactivity did occur there were differences between the commercial soy bean extracts and the extracts prepared from dust collected on site. There may be differences in the antigenic components of soy bean species from different countries, and locally manufactured RAST tests may be required. Variability in the allergen content of soy bean SPT samples could result from the methods used to prepare the extracts, selection of raw material, storage conditions, standardisation, quality and potency of extracts.[12] Human error and the interpretation of SPTs could also account for variability of results.

The poor association between tests of sensitisation and disease may be explained by factors associated with the subjects themselves. High levels of soy bean dust in the workplace are likely to produce symptoms caused by nonspecific irritation, in which case measures of specific IgE will clearly be inappropriate. The questionnaire as a measure of disease outcome is problematic when not supported by more objective methods. For example, workers may hide symptoms to protect jobs if diagnosis of a work-related condition may lead to dismissal. Tests for sensitisation may be associated with particular symptom complexes and disease, rather than with nonspecific symptoms consistent with allergic disease. A more targeted approach may thus be indicated.

Conclusion

In this study soy bean-specific IgE tests failed to identify workers with symptoms consistent with allergic disease. This does not necessarily mean that these tests are not useful, as many remedial factors may explain the disappointing results. The tests were associated with exposure, however, an important factor given that exposure may be denied or unknown.

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