

Occupational sensitization to lupin in the workplace: Occupational asthma, rhinitis, and work-aggravated asthma

Charlotte P. Campbell, MRCP,^a Abigail S. Jackson, MRCP,^a Anthony R. Johnson, FRACP,^b Paul S. Thomas, MD, FRACP, FRCP,^c and Deborah H. Yates, MSc, MD, FRACP, FRCP^{a,b} Sydney, New South Wales, Australia

Background: Lupin is a legume. Its seed can be ground into flour and incorporated into food as a protein source. Cases of rhinitis, urticaria, and anaphylaxis from ingestion of lupin have been reported as well as asthma.

Objective: To present a cross-sectional study of workers in a food processing company who were exposed to lupin and developed occupational allergy secondary to inhaling lupin products.

Methods: Subjects were interviewed using a standardized questionnaire, including demographics and current and past symptoms. They underwent skin prick tests (SPTs) to common aeroallergens and lupin products, spirometry, and off-line exhaled nitric oxide measurement. Symptomatic subjects, sensitized to lupin on SPT, underwent methacholine bronchial provocation challenge. Those with bronchial hyperresponsiveness had specific bronchial provocation challenge to lupin.

Results: A total of 53/54 subjects completed testing (98%). Overall, 21% (11/53) had positive SPT results to lupin. The lupin-sensitive group had a trend toward atopy ($P = .06$). Seven of 11 (64%) subjects in this group were symptomatic; all had rhinitis, and 2 had wheeze. Two subjects had positive methacholine challenges, and 1 had a positive specific bronchial provocation challenge to lupin with both an early-phase and a late-phase response.

Conclusion: Allergy to inhaled lupin occurs in the workplace. A high sensitization rate on SPT was found, which correlated with symptoms. The clinical significance of cross-reactivity between legumes on SPT is unclear.

Clinical implications: Sensitization to the legume, lupin, can occur from exposure at work and carries a high prevalence of clinical symptoms, which in some cases leads to occupational

rhinitis and asthma. (J Allergy Clin Immunol ■■■■;■■■: ■■■-■■■.)

Key words: Bronchial provocation challenge, hypersensitivity, occupational disease

Lupin is a flowering plant that forms part of the legume family, which also includes peas, lentils, beans, and peanuts. Australia is the world's largest producer of lupin beans, which grows approximately 75% of the total world lupin crop, primarily in Western Australia. Lupins were traditionally used as a nitrogen-fixing crop in rotation with wheat, restoring nitrogen to the soil, with the seeds used for cattle feed. Although some lupin seeds are poisonous, the toxic alkaloids responsible are absent in the sweet lupin, *Lupinus albus*, which is safe for human consumption.¹⁻³ Lupin kernels are high in protein (approximately 40% by weight) with high dietary fiber and low oil content. Human consumption of lupin products has been increasing in Europe, particularly France, because of consumer discomfort regarding genetically modified soy products and the culinary advantages that include use as an emulsifier and for producing smooth sauces. For animal consumption, lupin product has been suggested for a wide variety of uses ranging from plant-based fish nutrition to increasing testicular growth in rams. In Australia, lupin flour is already used to replace cereal grain in some products such as bread, biscuits, and pasta. Research is currently underway to develop palatable food products from lupin flour to cater to the health food market and to those with gluten sensitivity.

Recently, some reports have been published concerning allergy to lupin, particularly from France and Spain, where lupin is increasingly used in food products. Rhinitis, asthma, urticaria, and anaphylaxis have all been described,⁴⁻¹⁰ including 1 report documenting cases of anaphylaxis in Australia.¹¹ IgE serologic cross-reactivity between members of the legume family has been demonstrated in sensitized patients, although variable clinical significance occurs.¹² These scientific findings have led European parliament to call for lupin to be included as a potential food allergen in the European Union directive on food labeling.¹³

Incorporation of lupin product into human food, with the associated grinding, processing, and baking, has

From ^athe Department of Thoracic Medicine, St Vincent's Hospital, Darlinghurst, Sydney; ^bthe Dust Diseases Board Research and Education Unit, Sydney; and ^cthe University of NSW and Prince of Wales Hospital, Sydney.

Supported by the Lesley Pockley Research Fund.

Disclosure of potential conflict of interest: D. H. Yates has received grant support from Dust Diseases Board Scientific Grants, the Actelion Award, and Lesley Pockley Clinical Research Grants. The rest of the authors have declared that they have no conflict of interest.

Received for publication July 28, 2006; revised January 8, 2007; accepted for publication January 9, 2007.

Reprint requests: Deborah H. Yates, MSc, MD, FRACP, FRCP, Department of Thoracic Medicine, St Vincent's Hospital, Darlinghurst, NSW 2010, Australia. E-mail: Deborahh88@hotmail.com.

0091-6749/\$32.00

© 2007 American Academy of Allergy, Asthma & Immunology

doi:10.1016/j.jaci.2007.01.032

Abbreviations used

ATS: American Thoracic Society
 ERS: European Respiratory Society
 FeNO: Fractional exhaled nitric oxide
 FVC: Forced vital capacity
 MDI: Metered dose inhaler
 SPT: Skin prick test

increased the potential for sensitization, both by inhalation as well as by ingestion. Potential exposure and sensitization to lupin in the workplace could lead to occupational rhinitis and asthma, as well as anaphylaxis from ingestion of other legumes through cross-reactivity. Here, we report the first cluster in Australia of occupational sensitization to lupin by inhalation, which includes both occupational rhinitis and occupational asthma.

METHODS

This study was instigated after 3 index cases were referred to our asthma clinic. All worked in a food processing company and had been involved in the use of lupin product for human consumption.

Workplace screening

All workers with potential exposure to lupin ($n = 54$) were invited to participate in screening and gave informed consent as well as release of specific information on sensitization to the employer. Five individuals had initially been evaluated in the St Vincent's Hospital Asthma Clinic. The workplace screening was conducted over 2 separate consecutive days at the workplace during the working week. Each individual had all tests performed on the same day.

Subjects were interviewed by 1 of 4 doctors for the following details: demographics, lupin contact in the workplace, and current symptoms of hypersensitivity; clinical examination immediately followed.

The assessment of potential exposure was performed as follows:

1. An initial site inspection was carried out.
2. During the interview, workers gave their job title and indicated whether they worked in the open laboratory or in administration, as well as whether they believed that they were in contact with lupin.
3. Subjects were subsequently assigned to exposure categories, as described in Table I, using the information given regarding their job title, their contact with lupin, and the part of the building in which they worked:
 - a. No contact—worked in a different part of the building.
 - b. Indirect exposure—did not say they worked with lupin but had contact with the laboratory in which it was prepared.
 - c. Infrequent exposure—occasionally tested lupin or was occasionally exposed.
 - d. Lupin frequent exposure—tested lupin regularly or said they had frequent exposure.

Investigations performed were as follows:

1. SPT: Test was performed using the puncture method according to guidelines,¹⁴ with normal saline as negative control and positive control as 10 mg/mL histamine solution. Criteria for a positive SPT result were a wheal diameter greater than

or equal to 3 mm, with a negative control, after 15 minutes. SPTs were performed using standardized extracts of aeroallergens: cockroach, *Alternaria*, *Dermatophagoides farinae*, *Dermatophagoides pteronyssinus*, and cat hair (Hollister-Stier Laboratories, Spokane, Wash). Legumes were tested using standardized extracts of peanut and soybean (Hollister-Stier Laboratories); crude saline extracts were made of pea, chickpea, lentils, and lupin hull extract, as described by Smith et al.¹¹ Lupin flour, fiber, and protein were dissolved in a 1:10 solution 0.9% saline by weight. The lupin product was obtained from the company.

2. Spirometry: FEV₁ and forced vital capacity (FVC) were measured in triplicate using a MicroMedical Microlab spirometer, according to American Thoracic Society (ATS) guidelines.¹⁵ FEV₁ and FVC were measured from at least 3 and no more than 8 forced expiratory curves that had an acceptable start and end of test, were free of artifact (for example, cough), and were repeatable within less than 0.015 L for FVC and FEV₁. The largest FVC and the largest FEV₁ (BTPS) were recorded after examining the data from all usable curves. All subjects were successful in performing spirometry, which conformed to ATS/European Respiratory Society (ERS) specifications.
3. Fractional exhaled nitric oxide (FeNO) measurements: Offline FeNO measurements were performed according to ATS/ERS guidelines¹⁶ on site during the day of screening. Expired air was collected in impermeable reservoirs and gas contents were analyzed in the laboratory (LR2000, Rochester, United Kingdom [UK]) later on the same day.

Bronchial provocation testing took place in hospital laboratory according to ERS guidelines¹⁷ for patients with current symptoms and with positive SPT to lupin. Methacholine challenge testing was undertaken only in subjects who were symptomatic, who also had positive SPT results, and who consented to the test.

Bronchial provocation testing

1. Methacholine challenge: Methacholine challenges were performed using the dosimeter method.¹⁷ A baseline FEV₁ of greater than 70% predicted was required before challenge testing. Before testing bronchodilators, inhaled steroids and antihistamines were withheld according to guidelines.¹⁷ On the challenge day, the patient performed 3 baseline spirometry measurements. Normal saline was then inhaled from the nebulizer over 5 seconds using a breath-activated Mefar Dosimeter MB3 CE (Mefar, Brescia, Italy). It was repeated up to a total of 5 times without delay. After 2 minutes, spirometry was repeated in triplicate giving a postsaline baseline FEV₁. A FEV₁ fall of 20% from postsaline FEV₁ baseline measurement was taken as the endpoint for the challenge. The patient then inhaled doubling concentrations of methacholine from 0.06 mg/mL to 64 mg/mL using the same method, with FEV₁ performed after 2 minutes after each dose, until there was a 20% fall in FEV₁ compared with postsaline FEV₁. The patient was then given inhaled salbutamol 200 µg via a metered dose inhaler (MDI), and spirometry was checked 15 minutes after ensuring FEV₁ was 80% of baseline.
2. Specific bronchial provocation with lupin flour: Subjects with bronchial hypersensitivity were considered for specific bronchial provocation challenge testing with lupin flour, which was performed according to ERS guidelines.¹⁷ Briefly, SPT with doubling dilutions of lupin flour were performed to determine the skin prick endpoint, that is, the weakest concentration producing a wheal of greater than or equal to 2 mm,¹⁸ and thus decide the starting concentration of lupin flour for the bronchial challenge.

TABLE I. Lupin-sensitive patients: specific symptoms and SPT results

Subject no.	Exposure to lupin* (grades 0-3)	SPT result: wheal size (mm)					Atopy	Current clinical symptoms
		Flour	Hull	Fiber	Protein	Greatest†		
11	3	8	0	0	0	8	+	Wheeze, eyes, sneeze
14	3	9	3	3	5	9	+	Sneeze
20	3	8	4	13	10	13	+	Sneeze
23	3	0	3	1	0	3	—	Sneeze
25	3	3	1	1	1	3	+	—
27	0	3	3	0	0	3	+	—
34	3	4	4	0	3	4	+	Sneeze
35	3	7	3	5	16	3	+	Sneeze, eyes
37	1	6	0	2	6	6	+	—
46	1	3	0	0	1	3	—	—
53	3	8	0	0	8	8	+	Wheeze, eyes, sneeze

+, Present; —, absent.

*Grade of exposure defined as: 0 = no exposure known; 1 = indirect exposure, for example, laboratory next door; 2 = infrequent/occasional exposure; and 3 = sometimes or frequent exposure, such as grinding and weighing.

†Presence of symptoms correlated with size of the wheal to lupin ($P = .042$).

The specific bronchial provocation testing was performed in a single blinded manner, using the subject as his/her own control. First, a control day was given using normal saline, followed by a challenge day with aerosolized lupin flour by dosimeter method (Mefar Dosimeter MB3 CE) according to our protocol.¹⁹ An identical protocol was followed on the control day using normal saline alone as on the lupin flour day, with spirometry and FeNO measurements made at the same intervals. Baseline spirometry was performed to ensure FEV₁ greater than 70% predicted before testing.

Doubling dilutions were inhaled at 10-minute intervals until FEV₁ fell by 20% from postsaline FEV₁. Spirometry and FeNO were measured at 30-minute intervals during the second hour and then hourly up to the seventh hour. Salbutamol 200 µg via MDI was given if FEV₁ fell by 20%. The subject received written instructions about medical care for the next 24 hours.

Statistical analysis

This process was performed using SPSS 12.0.1 for Windows software (SPSS Inc, Chicago, Ill). The differences between lupin-sensitized subjects and nonsensitized subjects were compared with the following tests: Student *t* tests were used for parametric data, χ^2 tests for categorical data, and the Mann-Whitney *U* test for nonparametric data. *P* values less than .05 were taken as significant.

RESULTS

A total of 54 subjects were studied over 2 days. One subject was excluded from analysis as he was called away during workplace testing because of his work obligations and did not have time to complete SPTs. The participation rate was therefore 53 out of 54 or 98%.

Demographics

Characteristics of workers screened for lupin sensitization are shown in Table II, where comparison is made between the group with negative SPT results to lupin, that is, nonsensitized workers, and the sensitized workers with positive SPT to lupin.

TABLE II. Demographics of subjects not sensitized to lupin on SPT compared with those sensitized to lupin

	Nonsensitized to lupin (42)	Sensitized to lupin (11)
Age (y) (means $\pm$ SEs)	36.2 $\pm$ 1.7	39.6 $\pm$ 3.0
Male:female ratio	11:31 (74% F)	4:7 (64% F)
Smoker or exsmoker	4 (9.5%)	1 (9.1%)
Atopy*	21 (50.0%)	9 (81.8%)†
FEV ₁ (L) (means $\pm$ SEs)	2.84 $\pm$ 0.1	2.97 $\pm$ 0.2
Normal FEV ₁ /FVC ratio‡	40 (95.2%)	11 (100%)
FeNO (parts per billion) (means $\pm$ SEs)	5.9 $\pm$ 0.3	6.3 $\pm$ 0.5

*Atopy defined as ≥ 1 positive SPT result to aeroallergen at screening and excludes lupin SPT.† $P = .058$.‡Normal FEV₁/FVC ratio defined as $>70\%$.

Mean age and sex distribution were similar in the 2 groups. The number of smokers or exsmokers was low in both groups, compared with national figures of 21% for women and 26% of men in Australia,²⁰ but no significant difference was found between the 2 groups. No difference was found between the 2 groups with respect to spirometry (both mean FEV₁ and FEV₁/FVC ratio).

Atopy was present in 50% of nonsensitized workers, which compares with the national average of 44% in Australia.²¹ In the group sensitized to lupin, a trend toward more atopy than the nonsensitized group was observed, but this did not reach statistical significance ($P = .058$).

Clinical relevance

The most common allergic symptom reported by the subjects to any stimulus, not specifically to lupin, was sneezing, followed by runny eyes and then wheeze (Table III). The presence of any current allergic symptoms did correlate with sensitization to lupins on SPT ($P = .007$). The presence of current symptoms also correlated with

TABLE III. Comparison between subjects not lupin sensitized on SPT and lupin-sensitized subjects: current clinical symptoms of atopy to any stimulus and past symptoms of atopy

	Nonsensitized to lupin	Sensitized to lupin
Current symptoms of atopy/respiratory disease	9 (21.4%)* Itchy skin, 1 Sneezing, 3 Itchy throat, 1 Wheeze, 1 Cough, 2 Shortness of breath, 1	7 (63.6%) Sneeze only, 5 Sneeze, wheeze, and eyes, 2
Past symptoms of atopy/respiratory disease	17 (40.5%) Food allergy, 2 Eczema, 2 Sinusitis, 1 Tonsillitis, 1 Hay fever, 4 Asthma, 3 Bronchitis/shortness of breath, 4	6 (54.5%) Hay fever, 2 Asthma, 2 Hay fever, bronchitis, 1 Asthma/eczema/food allergy, 1

*Significant difference between nonsensitized and sensitized to lupin : $P = .007$.

the size of the wheal on SPT to any lupin in all subjects ($P = .036$), and within the lupin-sensitive group ($P = .042$); that is, the greater the reaction to lupin on SPT, the more likely the presence of current allergic symptoms. Atopy to aeroallergens on SPT during workplace screening did not correlate with the presence of current symptoms ($P = .12$) or the size of the wheal to lupin on SPT ($P = .47$). In addition, no difference was found between those sensitized to lupin and those nonsensitized with regard to a history of atopic symptoms to any allergen.

Lupin-sensitized group

Details regarding workers sensitized to lupin are shown in Table I. Lupin flour was the most common positive SPT result occurring in 10 out of 11 workers, followed by lupin protein, hull, and fiber in descending order. Seven out of 11 workers were sensitized to more than 1 lupin product on testing. Wheal size to lupin on SPT correlated with current symptoms ($P = .042$) but did not correlate with the degree of exposure to lupin, using the scale as shown in Table I.

Four workers who were sensitized to lupin had no symptoms at the time of screening, and 3 of these workers were sensitized despite no obvious exposure to lupins (they reported no or indirect exposure to lupins only in the workplace: 1 was a technical services manager, and 2 were microbiologists who worked separately from the lupin laboratory, although close by).

Specific cases

Four workers—subjects 11, 14, 35, and 53—with symptoms of allergy and positive SPT results to lupin volunteered for further testing and underwent methacholine bronchial challenges, of which 2 were positive. Subject 11 had a PC₂₀ FEV₁ of .049 mg/mL; subject 53 had a PC₂₀ FEV₁ of 4.66 mg/mL.

Subject 11, who had severe bronchial hyperresponsiveness, was still working. She gave a history of childhood asthma with mild asthma as an adult and was allergic to

a wide variety of aeroallergens. Over past 2 years, symptoms had become worse and were notable on the days she worked, resolving over the weekend and during a maternity leave. She worked as an analytical chemist, which would involve grinding lupin products. Subject 11 did not go on to specific challenge because of safety concerns: She had reacted to lupin SPT with wheeziness within 5 minutes of testing, although only a nonsignificant decrease in her FEV₁ occurred at the time of the SPTs (88% to 82% predicted).

Subject 53 had only mild bronchial hyperresponsiveness at the time of testing but had been off work for 4 months because of her symptoms. She had developed conjunctivitis, rhinitis, and wheeze for the first time when working with lupin, which involved unpacking lupin products and weighing them with a spatula. Her symptoms worsened during the day of work and improved over the weekends. Subject 53 went on to have a specific bronchial provocation test with lupin flour. A 1:5000 dilution produced a 40% drop in FEV₁ from postsaline baseline—PCallergen 1:5000 dilution (Fig 1). She also experienced a late asthmatic response, with a 28% drop in FEV₁. Her condition was therefore diagnosed as occupational asthma and rhinitis secondary to lupin.

Subject 14 and subject 35 had normal bronchial responsiveness on methacholine challenge. Both had noticed symptoms of rhinorrhoea and sneezing when working with lupin products and were found to have occupational rhinitis.

Three of the 7 subjects with lupin-positive SPT results, and symptoms when working with lupin, did not accept further testing (subjects 20, 23, and 34). They were allocated presumptive diagnoses of occupational rhinitis for the purpose of analysis.

Only 1 worker in the nonsensitized group (subject 21) reported current symptoms, itching in her throat, when working specifically with lupins despite negative SPT results to lupin.

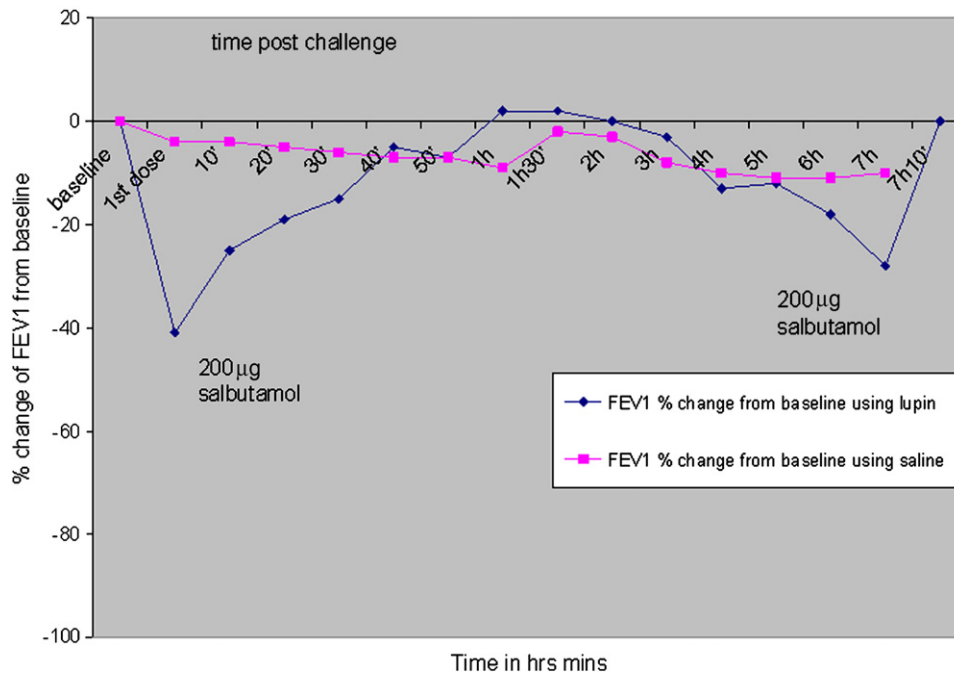


FIG 1. Specific bronchial provocation challenge with lupin flour (1 mg in 10 mL 0.9% normal saline diluted to 1:5000 using 0.9% normal saline) compared with control (0.9% normal saline). Changes in FEV₁ as a percentage of baseline are shown over time in hours and minutes.

TABLE IV. Cross-reactivity in SPT

Subject no.	Lupin-positive SPT	Current symptoms	Atopy on SPT*	Positive SPT to other legumes†	Clinical symptoms with food
4	No	None	No	Soybean	—
11	Yes	Wheeze	Yes	Peanut, soybean‡	Anaphylaxis to nonspecific food
14	Yes	Rhinitis	Yes	Pea	—
20	Yes	Rhinitis	Yes	Chickpea	—
34	Yes	Rhinitis	Yes	Peanut, pea	—
53	Yes	Wheeze	Yes	—	Oral tingling with peas

*Atopy defined as ≥ 1 positive SPT results to aeroallergens excluding lupins and legumes.

†Legume-positive SPT results correlated with lupin-positive SPT results ($P = .001$).

‡SPT performed elsewhere.

Cross-reactivity

Immunologic cross-reactivity between legumes on SPT was found in 4 subjects with lupin sensitivity (Table IV), compared with only 1 subject without lupin sensitization on SPT ($P = .001$). Subject 4 had significant SPT results to soybean but no other legumes or lupins. She was asymptomatic and did not show atopy to aeroallergens. Of the 4 lupin-sensitive subjects, only subject 11 has had a nonspecific food allergy, which was confirmed clinically by anaphylaxis on 2 occasions requiring treatment at hospital with adrenaline. The first episode had occurred 6 years ago, before working with lupins, and the second during the past year. Subject 53 reported symptoms of mouth tingling on ingestion of peas 2 years earlier, again before working with lupins, and has since avoided peas in her diet. However, at the time of testing, she had a negative

SPT result for pea. The other 2 subjects did not report any food allergies to legumes.

Exhaled nitric oxide

Exhaled nitric oxide levels were measured in all subjects (Table II). No correlation existed between exhaled nitric oxide levels and lupin sensitivity, atopy, or presence of symptoms.

Outcomes

The case of occupational asthma (subject 53) took sick leave and recovered significantly. She subsequently resigned and now works in alternative employment without significant asthma symptoms. The case of work-aggravated asthma (subject 11) has decided to leave because of her asthma symptoms. The other symptomatic

workers with rhinitis were moved to a different building (subject 35) and relieved from handling lupin flour (subject 14). Extraction fans have been placed in the lupin laboratory. The other 3 sensitized and symptomatic workers are still in the same employment as far as we are aware. The status of the other sensitized workers without symptoms is not known.

DISCUSSION

Two previous reports have focused on allergic rhinitis or asthma secondary to inhalation of lupin flour occurring in an occupational setting.^{23,24} Our study documents the largest group to date (53 workers) in a food processing factory involved in processing lupin products. We found a high prevalence of lupin sensitization on SPT—21%, which compares with the 29% prevalence in the previously published cross-sectional study of 7 lupin workers by Crespo et al.²³ We believe that clinical significance exists to lupin sensitization, as most of the sensitized group reported current symptoms of allergy, notably sneezing, when working with lupin products. Also, a significant correlation existed between current symptoms to any stimulus and lupin sensitization in all workers ($P = .007$), which was not present for atopy to aeroallergens alone, or a history of atopic symptoms. In addition, the larger the wheal size response to lupin on SPT, the more likely the presence of allergic symptoms ($P = .042$). Only 1 of 53 workers who did not have positive lupin SPT results complained of allergic symptoms when working specifically with lupin.

Lupin flour seemed to be the most potent allergen, causing sensitization in 10 of 11 of the positive workers, and therefore would be a good candidate for general screening by SPT in any future studies. Most sensitized workers were positive to more than 1 lupin product. The antigenic differences between different lupin products have not yet been fully investigated.

With regard to known risk factors for development of occupational asthma, we studied atopy, smoking, and exposure.^{22,25} We found a trend toward more atopy to aeroallergens in the lupin-sensitized group ($P = .058$). No difference in smoking habits existed between those sensitized and those not, although overall rates were low. We did not find a significant association between exposure and lupin sensitization or current symptoms, but most workers had some or frequent contact with lupin. The 2 cases of asthma were both frequent users of lupin, 1 weighing samples, whereas the other ground samples. However, some cases of lupin sensitization on SPT had very little exposure to lupin in the laboratory. The laboratory is open plan, and some workers walked into other areas wearing laboratory coats. All workers could therefore be exposed to respirable traces of lupin dust.

We expected that exhaled nitric oxide levels would reflect allergic responses, as FeNO has previously been shown to be raised in asthma, rhinitis, and atopy²⁶ and therefore might prove useful as a sensitive screening tool. However, we did not find an association between

nitric oxide levels and those who were atopic, had current symptoms, or were sensitized to lupin. However, the numbers in our study may have been insufficient to detect such an association and cannot be said to negate use of exhaled nitric oxide as a screening tool in this setting.

We identified 1 case of occupational asthma, 1 case of work-aggravated asthma, and 5 subjects with occupational rhinitis secondary to lupin inhalation. Some workers had not come forward before with their symptoms. Such underreporting is a common finding in occupational disease.² The outcome for the lupin-sensitized workers with no symptoms currently is unclear. Of these 4 workers, 3 seem to have low levels of exposure and do not work directly with lupin. Follow-up will determine whether symptoms develop later.

In 1994, Hefle et al⁴ reported the first documented case of lupin-induced food allergy. Cross-reactivity between members of the legume family has also been reported.¹² In particular, recent reports discuss food allergy to lupin on food challenge in peanut-sensitive individuals.^{6,9} The possibility of allergic symptoms from ingestion of lupin when sensitized to lupin by inhalation has been addressed previously with lupin allergy in the workplace,²³ where food challenges to lupin were positive in 2 workers sensitized to lupin by inhalation. In our study, we found several of the lupin-sensitized workers had positive SPT results to another legume, but this did not translate as far as could be determined into current clinical symptoms; no evidence of clinical cross-reactivity existed. Only subject 11 had had a nonspecified food-induced anaphylaxis in the past, with current positive SPT results to legumes. It would therefore have been of interest to perform double-blinded placebo-controlled food challenges to find evidence of clinical cross-reactivity rather than skin cross-reactivity, but food challenges were not available to us. This area deserves additional study. Another lupin-positive worker had symptoms of pea allergy in the past and now avoids pea, but the worker was not sensitive on SPTs at the time of testing. It is therefore not clear from this study what the clinical relevance of cross-reactivity between legumes on SPTs is in individuals with lupin allergies. It is theoretically possible that a person with previous legume food allergy may be at risk of development of lupin sensitization in the workplace, although the clinical relevance cannot be established from our study and has not been reported elsewhere.

In conclusion, our cross-sectional study found a high incidence of sensitization to lupin in a food processing company with various degrees of lupin exposure. Inhalation of lupin products in the workplace, particularly lupin flour, seems to be a potent cause of occupational sensitization. A significant proportion of workers will go on to develop occupational allergic rhinitis and asthma, but the clinical relevance of lupin positivity on SPTs remains undetermined. Occupational asthma remains as a preventable cause of morbidity, and studies such as ours show that novel substances such as lupin, which are used in an attempt to prevent allergic reactions, can themselves become allergens in the workplace leading to rhinitis, asthma, and possible food allergy.

We thank Dr William Smith (Royal Adelaide Hospital, Adelaide, Australia) for his help, particularly regarding lupin food allergy.

REFERENCES

1. Lamb CF, Cunningham DC. Australian Government Department of Fisheries and Forestry Rural Policy and Innovation: tracking potential GM inputs to the stock feed supply chain for feedlot beef 2003. Available at: http://www.affa.gov.au/corporate_docs/publications/pdf/innovation/scoping_study_gm_feedstuffs.pdf. Accessed July 2005.
2. Grieve M. A modern herbal: lupins. Available at: <http://www.botanical.com/botanical/mgmh/l/lupins50.html>. Accessed July 2005.
3. Murphy S. The many uses of lupins. Available at: <http://www.abc.net.au/landline/content/2006/S1631823.htm>. Accessed October 2006.
4. Hefle SL, Lemanske RF Jr, Bush RK. Adverse reaction to lupine-fortified pasta. *J Allergy Clin Immunol* 1994;94:167-72.
5. Novembre E, Moriando M, Bernardini R, Azzari C, Rossi ME, Vierucci A. Lupin allergy in a child. *J Allergy Clin Immunol* 1999;103:1214-6.
6. Moneret-Vautrin DA, Guerin L, Kanny G, Flabbee J, Fremont S, Morisset M. Cross-allergenicity of peanut and lupine: the risk of lupine allergy in patients allergic to peanuts. *J Allergy Clin Immunol* 1999;104:883-8.
7. Matheu V, de Barrio M, Sierra Z, Gracia-Bara MT, Tornero P, Baeza ML. Lupine-induced anaphylaxis. *Ann Allergy Asthma Immunol* 1999;83:406-8.
8. Gutierrez D, Conde A, Duran S, Delgado J, Guardia P, Martinez R, et al. Contact urticaria from lupin. *Contact Dermatitis* 1997;36:311.
9. Radcliffe M, Scadding G, Morrow Brown H. Lupin flour anaphylaxis. *Lancet* 2005;365:1360.
10. Faeste CK, Lovik M, Wiker HG. A case of peanut cross allergy to lupine flour in a hot dog bread 2004. *Int. Arch Allergy Immunol* 135:36-9.
11. Smith WB, Gillis D, Kette FE. Lupin: a new hidden food allergen. *Med J Aust* 2004;181:219-20.
12. Bernhisel-Broadbent J, Sampson HA. Cross-allergenicity in the legume botanical family in children with food hypersensitivity. *J Allergy Clin Immunol* 1989;83:435-40.
13. Report on the proposal for a European Parliament and Council Directive amending directive 2000/12/EC as regards indication of the ingredients present in foodstuffs COM(2001) 433-C5-0405/2001-2001/0199: COD/2001/0199 by the Committee on the Environment, Public Health and Consumer Policy, A5 0139-2002. Available at: http://www.europarl.eu.int/plenary_en.htm#reports. Accessed July 2005.
14. Bernstein IL, Storms WW. Practice parameters for allergy diagnostic testing. Joint Task Force on Practice Parameters for the Diagnosis and Treatment of Asthma. The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology. *Ann Allergy Asthma Immunol* 1995;75:543-625.
15. Anonymous. Standardization of Spirometry, 1994 Update. American Thoracic Society. *Am J Respir Crit Care Med* 1995;152:1107-36.
16. Anonymous. Recommendations for Standardised Procedures for the Online and Offline Measurements of Lower Respiratory Nitric Oxide and Nasal Nitric Oxide in Adults and Children—1999. *Am J Respir Crit Care Med* 1999;160:2104-17.
17. Sterk PJ, Fabbri LM, Quanjer PH, Cockcroft DW, O'Byrne PM, Anderson SD, et al. Airway responsiveness. Standardized challenge testing with pharmacological, physical and sensitizing stimuli in adults. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl* 1993;16:53-83.
18. Cockcroft DW, Murdock KY, Kirby J, Hargreave F. Prediction of airway responsiveness to allergen from skin sensitivity to allergen and airway responsiveness to histamine. *Am Rev Respir Dis* 1987;135:264-7.
19. Yates DH, Worsdell M, Barnes PJ. Effect of an inhaled glucocorticosteroid on mast cell and smooth muscle beta 2 adrenergic tolerance in mild asthma. *Thorax* 1998;53:110-3.
20. Clinical practice guidelines for the prevention, diagnosis and management of lung cancer. Australian Government: NHMRC and Cancer Council; 2004. p. 7.
21. Peat JK, Gray EJ, Mellis CM, Leeder SR, Woolcock AJ. Differences in airway responsiveness between children and adults living in the same environment: an epidemiological study in two regions of New South Wales. *Eur Respir J* 1994;7:1805-13.
22. Venables KM, Davison AG, Newman Taylor AJ. Consequences of occupational asthma. *Respir Med* 1989;83:437-40.
23. Crespo JF, Rodriguez J, Vives R, James JM, Reano M, Daroca P, et al. Occupational IgE-mediated allergy after exposure to lupine seed flour. *J Allergy Clin Immunol* 2001;108:295-7.
24. Parisot L, Aparicio C, Moneret-Vautrin DA, Guerin L. Allergy to lupine flour. *Allergy* 2001;56:918-9.
25. Balmes J, Becklake M, Blanc P, Henneberger P, Kreiss K, Mapp C, et al. American Thoracic Society Statement: occupational contribution to the burden of airway disease. *Am J Respir Crit Care Med* 2003;167:787-97.
26. Kharitonov SA, Barnes PJ. Clinical aspects of exhaled nitric oxide. *Eur Respir J* 2000;16:781-92.