

Immunological and Respiratory Findings in Spice-Factory Workers¹

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Immunological and respiratory findings were studied in a group of 45 female spice-factory workers (mean age: 39 years; mean exposure: 17 years). In addition a group of 45 female control workers matched by sex, age, and smoking habit were also studied. Intradermal skin testing with mixed spice dust allergen demonstrated positive skin reactions in 73.3% of exposed and in 33.3% of control workers ($P < 0.001$). Increased IgE serum levels were found in 36.8% of exposed and in 9.7% of the control workers ($P < 0.01$). The prevalence of chronic respiratory symptoms was significantly higher in the exposed workers than in the control workers ($P < 0.01$). There was, however, no consistent correlation between skin reactivity and chronic respiratory symptoms. There was a high prevalence of acute symptoms during the work shift. These complaints were more frequent in workers with positive skin tests for the symptoms of cough, chest tightness, and irritated and dry throat. Ventilatory capacity was measured by recording maximum expiratory flow-volume (MEFV) curves. There were statistically significant mean reductions during the work shift for all measured lung function parameters in workers with positive skin reactions. In those workers with negative skin reactions only FEF50 and FEF25 reached statistical significance. Aqueous extracts of different spices (chilli pepper, paprika, caraway, coriander leaves, coriander seeds, cinnamon, ginger, onion, curry, and parsley) caused a dose-related contractile response of isolated guinea pig tracheal smooth muscle. These data suggest that immunologic reactions to spices are frequent in spice workers and may be related to acute symptoms and lung function changes, but not to chronic changes. The data further suggest that, in addition to any immunologic response these spices may produce *in vivo*, they probably also provoke direct irritant reactions in the airways as suggested by *in vitro* data. © 1988 Academic Press, Inc.

INTRODUCTION

There is currently an increasing interest in diet and nutrition in general, and in potentially adverse reactions to food and food additives, in particular. The concept that certain foods may produce hypersensitivity reactions in susceptible individuals is widely accepted. However, there are only sporadic reports in the literature about spices. Most reports deal with classic allergic reactions. Aromatic plants, such as celery and parsley, have been reported by Kauppinen *et al.* (1980)

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to cause severe attacks of angioedema and urticaria in atopic patients. All of these patients ($n = 14$) showed positive skin reactions to celery and 12 patients had positive responses to parsley. Occupational asthma following the inhalation or the ingestion of garlic has been reported in atopic patients (Falleroni *et al.*, 1981; Lybarger *et al.*, 1982). Grinding of dried red chillies into a fine powder has been implicated as the cause of respiratory symptoms particularly in environments heavily contaminated with chilli powder (Uragoda, 1967). A burning sensation of the skin has also been reported in most of these workers, especially when the skin is moist. Occupational exposure to paprika dust has been associated with the development of hypersensitivity pneumonitis "paprika splitter's lung" (Fink, 1973). Lundberg *et al.* (1983) found that substance P and capsaicin (an active ingredient in chilli and paprika) induced a dose-dependent contraction of human segmental bronchi *in vitro*. Furthermore, the inhalation of capsaicin caused dose-dependent coughing in normal volunteers and in subjects with mild asthma (Collier *et al.*, 1984). The cough response documented in these subjects was not altered by the prior administration of sodium cromoglycate. Toorenenbergen and Dieges (1985) demonstrated that the inhalation of dust from spices results in an IgE-mediated allergy to these materials. Toorenenbergen and Dieges (1984) also described two patients working in a greenhouse with paprika plants. They documented that 58.7 and 43% of the total amount of histamine from washed leukocytes was due to challenge with paprika flower, leaf, and steam extract. In these patients serum IgE antibodies against paprika leaves and flowers could be demonstrated by the RAST test. Asthma and other symptoms in cinnamon workers have been described by Uragoda (1984), while Calnan (1976) reported six patients who developed an allergic contact dermatitis from the use of antiseptic ointment containing oil of cinnamon. Suhonen *et al.* (1979) reported skin tests, nasal and bronchial challenge tests, and RAST tests positive to coriander in a woman occupationally exposed to powdered coriander. Gohte *et al.* (1983) reported that in 28% of workers employed in preparing and distributing plant products, used in spices and as an ingredient in "health foods," had positive skin-prick tests or RAST tests against buckwheat; these workers also had work-related symptoms. Niinimäki and Hannuksela (1981) demonstrated positive skin reactions in atopic and nonatopic patients and found that paprika, coriander, caraway, cayenne, and mustard were responsible for the vast majority of these skin reactions. Additionally Niinimäki (1984) described positive skin tests to Jamaican pepper and cinnamon among patients referred to a dermatology clinic.

Despite this extensive anecdotal experience with spices and allergy there are no currently available epidemiological data on the effect of spices on the respiratory system. Moreover there are no studies on how immunologic reactions to spices might affect the airways. This current study includes research on respiratory symptoms, ventilatory capacity, and immunologic reactions in workers occupationally exposed to spice aerosols. Furthermore in order to understand the mechanism of potential airway effects caused by spice dust inhalation we studied this problem *in vitro* using isolated guinea pig trachea treated with extracts of different spices.

SUBJECTS AND METHODS

I. Epidemiological Study

Occupational exposure. Spices are the dried parts of various plants cultivated for their aromatic, pungent, or otherwise desirable components. Spices are used as adjuncts to impart flavor and aroma or piquancy to food and beverages. They have little or no nutritive values, but they stimulate the appetite, add zest to food, and enhance the taste. Among the most frequently used spices are chilli pepper, celery, caraway, cinnamon, coriander, garlic, mace, onion, paprika, parsley, and pepper. After harvest and collection, spices are cleansed of extraneous matter, cured if necessary, dried, sorted, and graded.

Our workers were exposed to spice aerosols during grinding, sifting, mixing, and packaging of different spices. These spices were prepared for incorporation into a mixed spice. The plant is located in Koprivnica, Yugoslavia, a small town in a rural part of the country.

Subjects. The study included a group of 45 female workers employed in a plant which manufactured a spice mixture composed of multiple natural vegetable ingredients. Workers were recruited as volunteers in this study. Of those available for study 80% participated. These represented those workers in the factory that were available for participation at the time of the study. A total of 92 workers are employed at the factory, but absence, vacation, or sick leave were the reasons for the majority of those not participating in the study. The mean age of the workers was 39 years (range, 25–48 years), the mean weight 69 kg (range, 55–78), mean height 159 cm (range, 149–169) and the mean duration of their industrial exposure was 17 years (range, 1–29 years). Seven percent of the workers were light smokers. These workers were exposed to a mixture of spices containing dried vegetable material, chilli pepper, paprika, pepper, parsley, garlic, onion, parsnip, ginger, turmeric, salt, and dextrose. A group of 45 female workers employed in packing bottles with fruit juice was used as a control. They were matched by sex, age, and smoking habit with the exposed group.

The spice industry has a high worker turnover rate. It is therefore not possible to say whether a healthy worker effect exists in this group. On average, however, those workers studied had been employed for an average of 17 years. Factors such as job type, length of exposure, and use of respiratory protection could not be evaluated in detail.

Immunological study. Intradermal skin tests were performed with an aqueous extract of a mixture of spices in exposed and in control workers. Spice allergen was prepared using standard immunologic techniques employing the dust collected in the workroom where workers were examined (Sheldon *et al.*, 1967). In addition, exposed workers were skin-tested separately with different antigens of individual spices such as chilli pepper, paprika, celery, ginger, parsnip, onion, pepper, and turmeric. Intradermal skin tests with these allergens were performed using a dilution of 1:500 (0.2 ml of solution). Workers were also tested with a standard aqueous extract of house dust, histamine base (0.01 mg/ml), and a buffer as a control solution. Skin reactions were read after 20 min. An intradermal skin

test was considered positive if the diameter of the observed wheal was >9 mm (corrected for the control reaction). The serum level of total IgE immunoglobulin was determined by a reference laboratory PRIST (Pharmacia Diagnostics AB Upsala, Sweden) using the direct radioimmunologic "sandwich" technique. Levels of IgE below 125 IU/ml were considered normal.

Respiratory symptoms. Chronic respiratory symptoms were recorded using the British Medical Research Council Committee questionnaire on respiratory symptoms with additional questions on occupational asthma (1960). In all workers a detailed occupational history as well as questions about their smoking habits were recorded. The following definitions were used:

Chronic cough or phlegm: cough and/or phlegm production for at least 3 months per year.

Chronic bronchitis: cough and phlegm for a minimum of 3 months a year and for not less than 2 successive years.

Dyspnea grades: grade 3, shortness of breath when walking with other people at an ordinary pace on level ground; grade 4, shortness of breath when walking at their own pace on level ground.

Occupational asthma: recurring attacks of dyspnea, chest tightness and pulmonary function impairment of the obstructive type diagnosed by physical examination and spirometric measurements during exposure to dust at or following work (WHO, 1986).

In all workers, the presence of acute symptoms during the work shift such as cough, dyspnea, chest tightness, irritation or dryness of the throat, secretion, dryness or bleeding of the nose, and headache were specifically recorded.

Ventilatory capacity. Ventilatory capacity was measured by recording maximum expiratory flow-volume (MEFV) curves using a portable flow-volume spirometer (Pneumoscreen, Jaeger, West Germany). Measurements were performed on the first working day of the week (Monday) before (6 AM) and after (2 PM) the work shift. The forced vital capacity (FVC), forced expiratory volume in 1 sec (FEV_1) and maximum flow rates at 50% (FEF_{50}) and 25% (FEF_{25}) of the control vital capacity were measured on these curves. At least three MEFV curves were recorded and the best value was used as the result of the test. The measured Monday preshift values of ventilatory capacity were compared with the expected normal values of Commission des Communautés Europeennes (CECA, 1971) for the FVC and FEV_1 and of Cherniack and Raber (1972) for FEF_{50} and FEF_{25} .

Environmental measurements. Airborne dust was sampled during an 8-hr work shift in the work places of the examined workers (mixing and packing of different spices). Casella personal samplers with Millipore field monitors and Millipore AA membrane filters were used to estimate total dust exposure. In addition, two stage stationary samplers, consisting of a membrane filter preceded by a horizontal elutriator, were used to collect the respirable fraction.

Statistical analysis. The results of ventilatory capacity measurements were analyzed by using the *t* test for differences of paired (acute effects across shift) and unpaired (comparing baseline to predicted values) variables. The χ^2 test (or where appropriate, Fisher's exact test) was used for testing differences in the

prevalence of respiratory symptoms; $P < 0.05$ was considered statistically significant.

II. In Vitro study of Spice Extracts

The effect of extracts of different spices was studied on isolated guinea pig tracheal rings. The spices which were tested included chilli powder, paprika, caraway, coriander leaves, coriander seeds, cinnamon, garlic, pepper, curry, parsley, and onion. Spice extracts were made by placing 1 g of the given spice in 10 ml of sterile water for 24 hr at a temperature of $+4^{\circ}\text{C}$. The solution was filtered through a sterile gauze sponge and centrifuged at 16,000 rpm for 20 min. The supernatant was decanted and used as the extract for the experiment.

We used the tracheas of young albino Hartly male guinea pigs (300–390 g) purchased from Perfection Breeders, Pennsylvania. Animals were sacrificed by CO_2 asphyxiation for 2 min and the trachea was removed within 3 min. The animal tissues were manually trimmed of excess fat and connective tissue. Four segments ("rings" each 4–6 mm wide) were cut from a single piece of trachea, and each was suspended between two L-shaped stainless-steel hooks mounted in a 20-ml organ chamber containing Krebs-Hanseliet buffer of the following composition (μM): NaCl, 110.0; KCl, 4.80; CaCl_2 , 2.35; MgSO_4 , 1.20; KH_2PO_4 , 1.20; NaHCO_3 , 25.0; dextrose 11.0; and Na_2EDTA , 0.03, in glass-distilled water. Organ chambers were maintained at $36.5 \pm 0.5^{\circ}\text{C}$, and were continuously aerated with 95% O_2 and 5% CO_2 to maintain pH, 7.5 ± 0.1 . The tissue segments were initially set to 2g of tension and were allowed to relax for approximately 1.5 hr before the experiment began. During that period the tissue was washed at 15-min intervals. After the relaxation period, the tension in each tissue segment was adjusted to 2g for all subsequent assays. Isometric contractions were recorded using a Grass FTO3C force displacement transducer attached to a Grass polygraph recorder. Before and after, concentration-response assays with our extracts of spices were performed, a challenge with carbachol 10^{-5} M was run. A dose-response curve with spice extracts was obtained by adding progressively increasing volumes of each extract or Krebs (used as a control) into the tissue bath in random order: 30, 50, 100, 300, 500, 1000, and 2000 μl . The potency of the extracts was determined by comparing their biological activity with the maximal contraction induced by carbachol (10^{-5} M) on the same tissue. The data expressed are a percentage of the initial maximal carbachol contraction (10^{-5} M).

RESULTS

I. Epidemiological Study

Immunological study. The results of intradermal testing have shown that all workers in this study had positive skin reactions to histamine (100.0%) and none reacted to buffer solution. Among exposed workers 73.3% reacted to the mixture of spices antigen, a significantly larger number than among control workers (33.3%) ($\chi^2 = 11.8$, $P < 0.001$). Separate skin tests with different spices in exposed workers demonstrated that the most frequent positive dermal reactions

occurred to chilli pepper (13.3%), followed by paprika and parsnip (11.1%), pepper and turmeric (6.7%), and onion and ginger (2.2%). The difference in skin test prevalence was significant between chilli pepper and ginger ($P < 0.01$). Among the control workers only 1 of 45 reacted to individual allergens, specifically with extract of chilli pepper.

Increased IgE serum levels were found in 36.8% of the exposed and in 9.7% of the control workers ($\chi^2 = 7.1$, $P < 0.01$). Among skin test negative workers all had low (normal) serum IgE. Of the 33 workers with positive skin tests, 16 had high IgE levels and 17 had low IgE levels.

Respiratory symptoms. The prevalence of chronic respiratory symptoms in exposed and in control workers is shown in Table 1. The prevalence of all symptoms was significantly higher in spice-factory workers than in control workers ($P < 0.01$). Among exposed workers, the highest symptom prevalences were obtained for nasal catarrh (37.8%) and dyspnea (35.6%), followed by chronic cough (31.1%), chronic phlegm and chronic bronchitis (28.9%), and sinusitis (22.2%). No case of occupational asthma was recorded in the exposed or in the control group. Figure 1 presents the prevalence of chronic respiratory symptoms in spice-factory workers with positive and negative skin tests to the mixture of spice antigens. There was no association between skin tests and chronic respiratory symptoms. In fact, for most of the chronic respiratory symptoms the prevalence was consistently higher among workers with negative skin tests than among those with positive skin tests (except for sinusitis). In subjects with positive skin tests the highest prevalences were found for nasal catarrh (36.4%), sinusitis (27.3%), and chronic cough (22.7%) while in workers with negative skin tests the highest prevalences were found for dyspnea (50.0%), followed by nasal catarrh and chronic cough (41.2%), and chronic phlegm and chronic bronchitis (33.3%). The prevalence of symptoms in both subgroups of workers was higher than among controls.

The prevalence of acute symptoms is presented in Fig. 2 in workers with positive and negative skin tests to the mixture of spices antigens. The only significant differences in prevalence between these two groups was obtained for dry throat (14 skin test positive workers: 31.3%; 0 skin test negative workers: 0%) ($P = 0.05$). These symptoms were found only in those workers with a positive intradermal skin test to the mixture of spice antigens. Additionally 38% of the workers complained of dermatologic problems related to spice dust exposure.

Ventilatory capacity. Table 2 shows the ventilatory function data separately in workers with positive and negative intradermal tests to the mixture of spice antigens. Workers with positive skin tests demonstrated significant mean across-shift reductions for all tests (FVC, -4.1%; FEV₁, -4.5%; FEF₅₀, -16.1%; FEF₂₅, -24.9%). By contrast, in workers with negative skin tests (FVC, -1.7%; FEV₁, -2.6%; FEF₅₀, -15.7%; FEF₂₅, -24.3%), statistical significance was only demonstrated for FEF₅₀ and FEF₂₅ ($P < 0.05$). Examining baseline (prework week) lung function in relation to normal values, there was no significant difference between mean Monday morning measured and predicted normal values, except for FEF₂₅ ($P < 0.01$). Mean values of FVC, FEV₁, and FEF₅₀ were greater than 80% of expected normal values, except for FEF₂₅ (77.1%) in workers with positive skin tests to mixture of spices. By analyzing individual measured data in

TABLE 1
PREVALENCE OF CHRONIC RESPIRATORY SYMPTOMS IN SPICE-FACTORY WORKERS

Group	N	Mean age (year)	Mean exposure (year)	Chronic cough (%)	Chronic phlegm (%)	Chronic bronchitis (%)	Asthma (%)	Dyspnea	Nasal catarrh (%)	Sinusitis (%)
Spice-factory workers	45	39 ± 9	17 ± 7	14 (31.1%)	13 (28.9%)	13 (28.9%)	0 0%	16 (35.6%)	17 (37.8%)	10 (22.2%)
Control workers	45	39 ± 9	16 ± 9	3 (6.7%)	2 (4.4%)	2 (4.4%)	0 0%	3 (6.7%)	2 (4.4%)	2 (4.4%)
P ^a				0.003	0.002	0.002	NS	0.0007	0.00008	0.01

^a Level of significance (P value) as determined by Fisher's exact test.

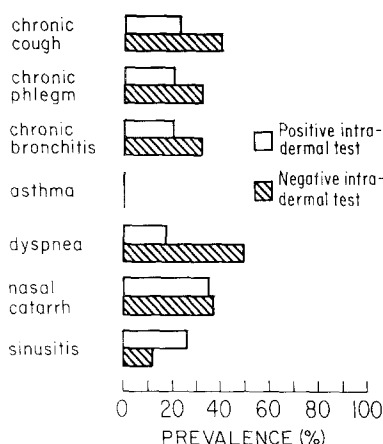


FIG. 1. Prevalence of chronic respiratory symptoms in 45 spice-factory workers by the presence of positive intradermal skin tests to a mixture of spice allergens.

relation to predicted values there were 2 (4.4%) workers with actual values less than 80% of predicted for FVC, 4 (8.9%) for FEV₁, 10 (22.2%) for FEF₅₀, and 20 (44.4%) for FEF₂₅. When comparing workers with positive and negative skin tests there were no differences in the frequency of abnormal baseline tests.

Environmental measurements. The mean dust concentration for total dust measured in the workplace was 2.9 mg/m³ (range, 0.5 to 10.1 mg/m³). The mean respirable fraction was 2.0% of the total dust. The highest concentrations of total

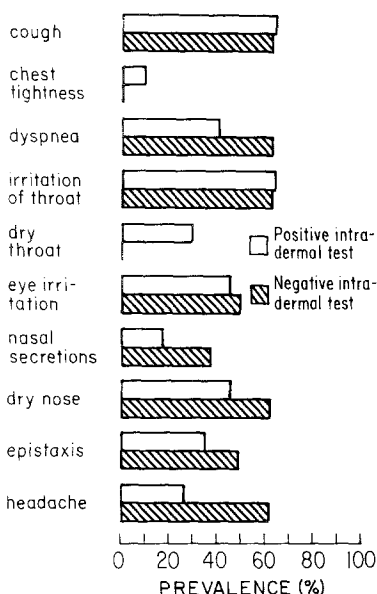


FIG. 2. Prevalence of acute symptoms during work shift in spice-factory workers by the presence of positive intradermal skin tests to a mixture of spice allergens.

TABLE 2
VENTILATORY CAPACITY IN SPICE-FACTORY WORKERS BY SKIN TEST RESULTS

Test	Positive intradermal test ($N = 33$)				Negative intradermal test ($N = 12$)			
	Before shift $\bar{x} \pm SD$	Difference before-after ^a		% of normal	Before shift $\bar{x} \pm SD$	Difference before-after		% of normal
		%	P			%	P	
FVC (L)	3.41 ± 0.47	-4.1	<0.01	101.2	3.52 ± 0.34	-1.7	NS ^b	102.5
FEV ₁ (L)	2.88 ± 0.44	-4.5	<0.05	107.6	3.04 ± 0.35	-2.6	NS	111.4
FEF ₅₀ (L/s)	4.16 ± 1.01	-16.1	<0.01	90.8	4.78 ± 0.71	-15.7	<0.05	100.8
FEF ₂₅	1.89 ± 0.77	-24.9	<0.01	77.1	2.30 ± 0.80	-24.3	<0.05	92.5

^a Across-shift changes in respiratory function.

^b NS, difference not statistically significant ($P > 0.05$).

dust were found in the areas of mixing different spices together. However, all workers were involved in different processes during work.

II. In Vitro Study of Spice Extracts

The mean data for the effect of individual spice extracts on guinea pig isolated tracheal smooth muscle are shown in Figs. 3a–3c. The results are presented as a percentage of an initial maximal carbachol contraction produced by stimulation with 10^{-5} M carbachol. When possible, dose-response parameters were calculated using a curve fitting the software of PROPHET (Boston, MA). These parameters, E_{MAX} , slope, and EC_{50} are detailed in Table 3.

Aqueous extracts of all spices except pepper and garlic increased the tone of tracheal rings inducing a dose-related smooth muscle contraction. The smallest maximal contractile activity was found for celery (26.5%) and the greatest for cinnamon (127.3%). Fig. 3a presents the dose-response data for spice extracts which caused increases of basal tension of up to 50% of maximal carbachol contraction at the highest dose tested. These included celery (26.5%), coriander leaves (31.3%), caraway (39.3%), and onion (48.1%). All of these extracts were added to the organ bath in aliquots of 30 to 2000 μ l, except for caraway which elicited its maximal contraction (39.3%) at a volume of 500 μ l. Figs. 3b and 3c present the data for spice extracts that caused a maximal contraction greater than 50% of maximal carbachol (10^{-5} M) contraction. These spices include chilli pepper (53.8%), paprika (56.2%), ginger (62.5%), parsley (63.5%), coriander seeds (64.7%), curry (118.2%), and cinnamon (127.3%). Spice extracts were added into the organ bath in progressive volumes of 30 to 2000 μ l except for cinnamon, for which the maximal contraction (127.3%) was obtained at a volume of 500 μ l. Adding extracts of pepper and garlic did not result in a contractile effect, except for a very transient small constrictive effect at the largest volume (2000 μ l). A control Krebs solution added in the same volume into the organ bath did not cause changes in the basal tone of the guinea pig tracheal rings. Carbachol 10^{-5} M added into the organ bath at the end of the assay following most of the spice extracts caused smooth muscle constriction similar to the initial carbachol 10^{-5} M response. However, following the challenges with individual extracts of ginger,

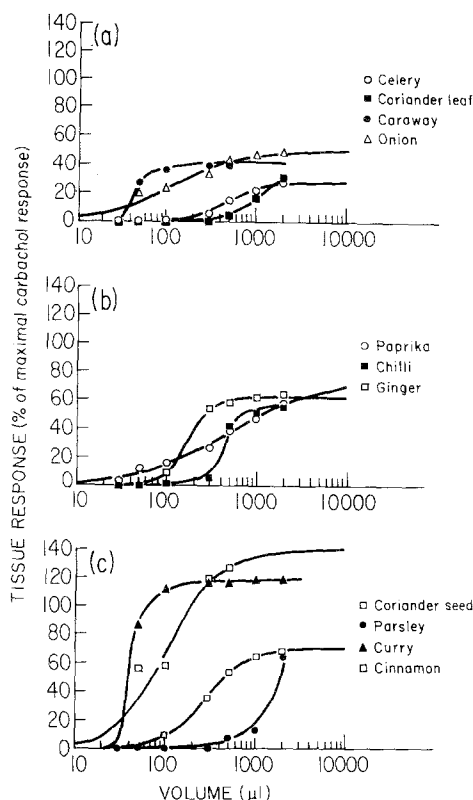


FIG. 3. Contractile activity of aqueous spice extracts on isolated guinea pig tracheal smooth muscle as percentage of initial carbachol 10^{-5} M contraction: (a) smaller than 50% of maximal carbachol contraction (celery, coriander leaves, caraway, onion); (b) and (c) greater than 50% of maximal carbachol contraction (chilli pepper, paprika, ginger, parsley, coriander seeds, cinnamon, curry).

chilli pepper, parsley, coriander seeds, and curry, the maximal carbachol (10^{-5} M) contraction was considerably increased in relation to the preassay carbachol 10^{-5} M contraction (range, 152.1 to 216.6%).

DISCUSSION

Our data both epidemiologic and *in vitro* suggest that aerosols of some spices have considerable biological activity on airways and may contribute to occupational illness. A significantly higher prevalence of chronic respiratory symptoms occurred in exposed workers than in control workers. Additionally acute reductions of ventilatory capacity over the work shift indicate that spices may be considered a noxious occupational substance causing reversible bronchoconstriction. These clinical findings are reinforced by our *in vitro* data.

Agents associated with occupational airway diseases have been classified into two categories: those associated with large molecular weight substances and those associated with smaller molecular weight agents (Murlas and Brooks, 1986). While food, food additives, herbs, and spices may act in many instances like

TABLE 3
EXTRAPOLATED RESPONSE PARAMETERS FOR DOSE-RESPONSE CURVES OF SPICE EXTRACTS^a

	$E_{\max}$ (% maximum carbachol)	Slope (% maximum carb/ μ l)	EC ₅₀ (μ l)
Coriander leaves	—	—	—
Celery	27.7	2.24	496
Caraway	37.5	0.75	35†
Onion	49.4	1.17	121
Chilli	55	0.25	400†
Paprika	73.4	0.84	506
Ginger	61.3	3.20	173
Parsley	—	—	—
Coriander seed	69.5	1.97	282
Curry	110	2.0	40†
Cinnamon	140	1.51	106

^a All parameters extrapolated by PROPHET algorithm for dose-response parameters, with the exception of † parameters which were estimates from tracings.

larger molecular weight allergens causing immunoglobulin IgE-mediated responses when ingested or inhaled, our study suggests that this is not the mechanism for many of their airway effects. While extensive sensitization clearly occurred in the spice workers involved in this study the data suggest that this is not a prerequisite for airway effects.

Bronchial provocation testing with coffee, tea, and cotton dust extract in workers or in healthy persons may cause a considerable decrease of ventilatory capacity indicating subjects sensitive to aerosols of a particular occupational agent(s) (Zuskin *et al.*, 1985a, 1985b; Schachter *et al.*, 1985). Acute reductions of ventilatory capacity in workers exposed to spice aerosols documented in this study were similar in magnitude to those of coffee and tea workers studied in the workplace (Zuskin *et al.*, 1979; Zuskin and Skuric, 1984). Our previous study (Zuskin *et al.*, in preparation) with disodium cromoglycate (DSC) in spice-factory workers demonstrated significant protection against the acute lung function reductions over the work shift following pretreatment with 40 mg of DSC. This is similar to our data in coffee workers where DSC significantly prevented bronchoconstriction during the processing of green coffee (Zuskin *et al.*, 1979). While DSC protection suggests that mediators from mast cells may be involved in the airway response, it does not necessarily in this situation imply an allergic IgE-mediated reaction; mediator release may be occurring through a non-IgE-mediated reaction. The present study has shown that 22.2% of workers had FEF₅₀ and 44.4% of workers had FEF₂₅ below 80% of predicted values, that is similar to the data in our previous study in spice-factory workers (23.9% of workers with FEF₅₀ and 53.3% of workers with FEF₂₅ below 80% of predicted normal values) (Zuskin *et al.*, in preparation). While this may indicate the early phase of chronic respiratory impairment, we did not document a significant proportion of workers with clinically significant lung function loss. Alternatively, it is well recognized that flow rates at low lung volumes have great variability; hence some of these findings may represent this increased variations.

Comparison of the Monday preshift (baseline) ventilatory capacity data with the predicted normal values demonstrated that only the mean FEF₂₅, in workers with positive skin tests to mixture of spices, was found to be below 80% of predicted. This again suggests that in the small group studied lung function changes were not associated with the development of immediate hypersensitivity. Other forms of immunologic response could nevertheless have occurred.

The study of Kauppinen *et al.* (1980) suggests that aromatic plants should be considered as a possible cause for severe allergic reactions. However, it has been noted that heating resulting from cooking of these products may inactivate the antigen or antigens mediating IgE responses. This may be one explanation for the tolerance of most individuals to ingested cooked spices. Toorenenbergen and Dieges (1987) analyzed specific IgE against the spices coriander, curry, mace, celery, and white pepper in patients with suspected food allergies and reported that IgE against these various spices may play a role in some adverse reactions to food. Spices are usually on the list of suggested elimination diets (Farrell, 1985). The percentage of spice-factory workers with positive skin reactions to a mixture of spices was considerably larger (73.3%) than the fraction of coffee workers (14.7%) and tea workers reacting to specific dust extracts (range, 11 to 23%). Increased serum levels of IgE in spice-factory workers were found in 36.8% of workers; higher than in tea workers (27%) or in coffee workers (24.4%). This suggests a greater sensitizing potential of these agents.

Our observation that large numbers of workers reported dermatologic problems is supported by other findings in the literature. Preparation of food in restaurant kitchens carries a high risk of occupational dermatosis, particularly from contact with onion and garlic (Hjorth and Roed-Peterson, 1976). Food handlers are sensitized by the proteins they touch, and then react to subsequent contact with these proteins. Bleumink *et al.* (1972) described a case of contact dermatitis to garlic with a positive patch test induced by a piece of garlic bulb and extract of garlic. Aqueous extracts of onion, garlic, and ginger have been found to inhibit platelet aggregation induced by ADP, epinephrine, collagen, and arachidonate in a dose-dependent manner *in vitro* (Srivastarva, 1984). However, in our study with isolated guinea pig trachea we did not find a bronchoconstrictor effect of garlic extract on isolated guinea pig smooth muscle trachea.

Our studies on isolated guinea pig trachea suggest that clinical respiratory findings obtained in humans can be simulated in guinea pig tracheal smooth muscle *in vitro*. Discrepancies between our findings *in vitro* and reported clinical data however are notable. Although we recorded the smallest constrictor effect with celery, Wutrich and Dietschi (1985) reported celery and carrot as frequent food allergens; not only in their raw form, but also cooked and as spices. Immunological investigation in an atopic patient who developed a marked adverse response to garlic revealed significant skin reactivity and bronchospasm after challenge with both garlic dust and extract (Lybarger *et al.*, 1982). In some instances the bronchoconstrictive effect of aqueous extract of spices has been more completely characterized. For example with chilli pepper and paprika the constrictory effect may be due to capsaicin present in these foods. Molnar *et al.* (1969) reported that capsaicin elicited constriction of isolated guinea pig tracheal rings.

We have shown that extracts of different spices have components that can

induce airway constriction in *in vitro* experiments by a direct action on guinea pig airway smooth muscle. The guinea pigs used in experiments were not presensitized to spices. Previous experience suggests that such airways are pharmacologically similar to human airway muscle (Brink *et al.*, 1980). This contractile activity is concentration dependent. These data are similar to the results obtained with extracts of green coffee dust on isolated guinea pig tracheal spirals (Zuskin *et al.*, 1983). It appears that the amount of biologically active material(s) calculated on the basis of the percentage of maximal carbachol contraction varied. This activity was greatest for cinnamon (127.3%) and smallest for celery (26.5%).

Many investigators consider that adverse reactions of workers to spice dust are allergic in nature. Our epidemiological study does confirm that specific atopy correlates with the severity of airway responses seen in the workplace. Nevertheless, airway symptoms both acute and chronic do not reflect skin testing results. This could suggest that immunologic reactions to spice extracts may not be specific for airway sensitivity and that further *in vivo* testing (e.g., bronchial provocation with specific antigens) may be required to establish a link between skin test reactivity and bronchial reactivity. Furthermore our *in vitro* studies point to a nonspecific bronchoconstricting effect of spice extract. Thus in addition to specific allergic reactions, spice dust may possibly induce airway disorders by a direct irritative action on airway smooth muscle, by reflex mechanisms or by both (Habib *et al.*, 1979).

We suggest that the dusty conditions in spice factories represents a highly efficient bronchoconstrictor challenge of the respiratory tract. In order to prevent acute and chronic respiratory illness in this environment, exposure to airborne contaminants should be controlled by methods of industrial hygiene such as enclosure of the process, removal of the contaminants at the source by local exhaust ventilation, limiting the number of susceptible workers exposed to the hazard, segregation of the process, and personal protection.

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