Asthmatic reactions to a commonly used aerosol insect killer

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ABSTRACT: Seven patients with asthma and a history of chest tightness on exposure to aerosol insecticide sprays were studied. Under controlled conditions, objective measures of airways narrowing were taken before and after exposure to an aerosol insect killer (Mortein Pressure Pak). Chest tightness described as asthma was produced in all seven subjects, but only one showed a greater than 20% fall in FEV_1, compared to baseline values. A further two subjects showed small changes in the maximum mid-expiratory flow rate. No changes were observed in the subjects' sensitivity to inhaled histamine before, and 24 hours after, exposure to the insecticide. Thus, exposure to a commonly used household insecticide spray produced marked symptoms in all subjects, but objective evidence of airways obstruction was present in only three, and no changes in bronchial reactivity to inhaled histamine occurred in any of the subjects.

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ON QUESTIONING about factors which provoke asthmatic attacks, many patients with asthma state that aerosol insect killers are major offenders. As early as 1923, Garratt and Bigger reported a case of asthma triggered by insect powder containing pyrethrum.[1] Since 1930, when Ramirez reported four cases of asthma triggered by pyrethrum,[2] there has been little investigation into this common symptom. However, cases of allergic rhinitis,[2] dermatitis,[3] and hypersensitivity pneumonitis[4] have been reported, indicating the ability of insect killers to produce an allergic reaction.

The objectives of our study were (i) to elicit whether a history of insect-killer-produced asthmatic attacks correlates with a change in lung spirometry in controlled provocation tests; (ii) to follow the time sequence of any asthmatic reaction that occurs; and (iii) to determine whether any variation in bronchial reactivity to histamine occurs after exposure to an insect killer.

Materials and methods

An aerosol insect killer was used in the challenge tests. The one chosen is non-toxic to humans, and is a popular brand of insect killer on the market. It is often named by patients with asthma as the culprit in triggering an asthmatic attack. The composition of the insect killer used (Mortein Pressure Pak insect killer) is: (*a*) *active ingredients* — 3.0 g/kg pyrethrins, 0.9 g/kg tetromethrin, 15 g/kg piperonyl butoxide and 7.5 g/kg *N*-octyl-bicycloheptene dicarboximide; (*b*) *propellants* — chlorofluorocarbons and hydrocarbons; and (*c*) *solvent* (non-water based).

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The spray rate for the insect killer was calculated by weighing the can before and after a 10-second spray. The scales used were accurate to 0.1 g. By means of this method, a spray rate of 1.59 g/s was obtained. Concentrations of the substance in a 7-m^3 room were calculated on the basis of 5-s, 10-s, 20-s and 30-s sprays. The maximum concentration reached in the room was 6.7 mg/L. This level was well below the toxic level indicated by the manufacturers,[5-7] but slightly higher than that which the average householder would encounter in the domestic usage of the insecticide.

Seven patients were selected for study on the basis of the following criteria: (*a*) proven bronchial asthma; (*b*) positive history of chest tightness on exposure to aerosol fly-killers; (*c*) aged between 18 and 75 years; (*d*) well controlled, mild or moderate asthma; (*e*) not pregnant or liable to be pregnant; and (*f*) no cardiac disease. Informed written consent was obtained before commencement of the trial. Patients were studied over several days.

Day 1

A full profile was obtained from all patients. This included a detailed history of their asthma, a full blood count, ESR, biochemical screen, testing for *Aspergillus* precipitins and skin-prick testing with common allergens.

Bronchial reactivity to inhaled histamine was determined by means of a Rosenthal French Nebulization Dosimeter model 2A attached to a De Vilbiss hand-held nebulizer No. 646. Before testing, patients did not inhale β_2-agonists, or corticosteroids or sodium cromoglycate for six hours, and did not take by mouth theophylline for 12 hours, slow-release theophylline for 24 hours, or antihistamines for 48 hours. No patient had suffered from a respiratory tract infection for one month before the challenge.

The forced expiratory volume in one second (FEV_1) was measured on a Godart Expirograph, 30 seconds and 90 seconds after five inhalations of 1.0 mL histamine, ranging in concentration from 0.3 mg/mL to 8 mg/mL. The concentration of histamine causing a 20% fall in FEV_1 was calculated (PC_{20}). This test is a

TABLE: Results of the study

	Patient profile			PC_{20}(mg/mL)†		Challenge				
						FEV_1 (L)		MMEFR (L/s)		
	Age (years) and sex	Atopic*	Aspergillus precipitins	Before challenge	After challenge	Baseline	Fall	Baseline	Fall	Symptoms of chest tightness
1	57F	+ 3/24	–	ND	ND	1.0	35%	1.22	60%	+
2	24F	+ 6/24	–	1.18	1.15	3.55	14%	3.3	24%	+
3	35F	+ 14/24	–	ND	ND	1.4	11%	1.09	25%	+
4	61F	+ 5/24	–	0.61	ND	1.25	12%	ND	ND	+
5	46F	–	–	3.48	3.48	1.2	8%	0.86	0	+
6	71M	–	–	1.82	1.0	2.2	9%	1.75	0	+
7	68M	–	–	6.06	8	2.3	0	3.4	0	+

* Number of positive reactions to skin-prick tests out of 24 performed.
† Bronchial reactivity to histamine (PC_{20} — the concentration of histamine which caused a 20% fall in FEV_1).
FEV_1 = forced expiratory volume in one second.
MMEFR = maximum mid-expiratory flow rate.
M = male. F = female. ND = not done. + = positive. – = negative.

measure of non-specific bronchial hyperreactivity, which is increased in 100% of patients with current asthma.[8] It has been shown to increase after exposure to ozone,[9] allergens,[10] SO_2,[11] and after respiratory infections.[12] By testing histamine reactivity before and after provocation with the insecticide, it was hoped to observe whether this substance had altered the reactivity, other factors being kept constant.

Provocation. — This took place in a 7-m^3 room which had large windows in one side to allow close observation of the patient. An exhaust fan removed fumes between sprays. After allowing the effects of histamine to wear off, the provocation took place as follows:

1. Three baseline readings, 15 minutes apart, of the forced expiratory volume in one second (FEV_1) vital capacity (VC), and maximum mid-expiratory flow rate (MMEFR, a measure of small-airways obstruction) were measured on a Vitalograph spirometer.

2. A five-second spray of the insecticide was delivered into the room and the patient then sat in the room for five minutes. The patient was unaware of the contents of the spray, as he or she was told that many different substances had been provided by the manufacturer. Immediately on leaving the room, spirometry was repeated. For the purpose of the study falls of 20% or more either in FEV_1, or in MMEFR, or both were considered as an indication of significant bronchoconstriction.

3. Spirometry was repeated after a further five minutes. If no asthmatic reaction had occurred, the procedure was repeated with 10-second, 20-second, and 30-second sprays of the insect killer.

If, at any time, a significant asthmatic reaction developed, the challenge was stopped, and spirometry was performed every five minutes until the readings returned to the baseline values.

If no significant asthmatic reaction developed after the 30-second spray, spirometric values were measured every five minutes for 30 minutes, then at 15-minute intervals for 30 minutes, and then every half-hour for at least two hours. Thus most patients were followed up for three hours after challenge.

Patients were allowed to go home on the day after airways function returned to normal. They were asked to report if any asthmatic reaction developed over the following 24 hours.

Day 2

The histamine provocation test was repeated. A twofold difference in PC_{20} was considered significant.

In those patients who developed a significant asthmatic reaction to the insect spray, provocation was repeated with a placebo (water). This was to ensure that the reaction was a specific one to the pressurized insect spray and not due to stress, repeated forced expiration, confinement in the provocation room, and so on.

Day 3

The patient was asked to inhale 2 mg of atropine methonitrate dissolved in 2 mL of water, using the same equipment as that used for the inhalation of histamine. After 60 minutes, provocation with the insect spray was carried out in the same way as on Days 1 and 2.

Results

The results are summarized in the Table. The aerosol insect killer produced symptoms in all patients. They complained of chest tightness, which they described as "asthma". This sensation usually began after one or two five-minute exposures in the provocation room and continued for up to one hour after challenge.

In six of the seven patients, this chest tightness was associated with a severe non-productive cough, sneezing, rhinorrhoea, and lachrymation; these symptoms usually resolved within five minutes after leaving the provocation room. However, one patient (Patient 5) coughed for about 30 minutes after a 10-second spray, while another (Patient 3) had rhinorrhoea and sneezing for about one hour after challenge.

Three patients showed some objective evidence of airways-narrowing. This was seen as a significant fall in their MMEFR. In two (Patients 1 and 2), the fall was maximal at 15 to 20 minutes after challenge. The reaction lasted about 45 minutes in Patient 2; in Patient 1, the MMEFR remained well below baseline for about 210 minutes after challenge, at which time the reaction was reversed. The third patient (Patient 3) had a maximal fall in MMEFR at 90 minutes after challenge. This continued for at least 270 minutes before the reaction was reversed. The falls in MMEFR in two of the three patients (Patients 2 and 3) were of such a small degree as to be only just significant by the criteria of this study. Only one patient (Patient 1) had a significant fall in FEV_1, which was maximal at 25 minutes after challenge. The reaction lasted 90 minutes (Table).

There were no significant changes in VC, FEV_1, or MMEFR in any of the other patients. None of the patients showed significant changes in lung-function values on the placebo day. The bronchial reactivity to histamine before and after provocation was tested in four patients (Table). For each patient, the testing occurred at the same time of day, 24 hours apart. There were no significant changes in the histamine reactivity after bronchial provocation with the insect killer.

The only patient to show a significant fall in FEV_1 (Patient 1) returned on a third day and underwent provocation 60 minutes after inhalation of 2 mg of atropine methonitrate. The patient experienced chest tightness and coughing, as during the challenge on Day 1. There was a significant fall both in MMEFR (41% fall) and in FEV_1 (20% fall), and this reaction was again maximal about 15 to 20 minutes after challenge; the time sequence was similar to that in the previous reaction.

Discussion

It is evident from this study that a complaint of chest tightness in subjects with asthma on exposure to the aerosol insect killer does not necessarily correlate with objective changes in spirometry. Even in those who developed an objective change in lung function, the sensation of chest tightness appeared long before the actual fall in spirometry readings occurred. Other workers have also commented on this disparity. Golden *et al.* stated that studies of exposure to ozone (0.1 ppm to 1.0 ppm) have shown only small and evanescent effects on pulmonary function, even though many of the participants in these studies complained of coughing, chest tightness, substernal soreness, and shortness of breath after exposure.[9] They claim that this disparity has been a puzzling feature of research on the effects of ozone and other air pollutants on pulmonary function.

The nature of the symptoms suggests that irritant receptors in the tracheobronchial tree are being stimulated. These receptors are myelinated nerve fibres which branch beneath the epithelium and within its base. They send twigs between the columnar cells towards the surface, ending beneath desmosomes or tight junctions. Experiments have shown that stimulation of these receptors produces cough, bronchoconstriction, and hyperpnoea.[13] Depite apparent stimulation of these receptors in all patients in our study, as evidenced by cough, substernal soreness, and chest tightness, a fall in FEV_1 occurred in only one subject. This is a puzzling feature of the study. The effect of the aerosol insect killer appeared to be mainly on the smaller airways, as measured by the MMEFR. The reaction was immediate and lasted up to several hours. No late asthmatic responses were noted.

The mechanism of this reaction is still unclear. Inhalation of 2 mg of atropine methonitrate modified, but did not block, the asthmatic reaction in the one patient tested. The effect of this drug is to block the vagus nerve. This should prevent the occurrence of an asthmatic reaction mediated by the parasympathetic nervous system. The fact that it did not do so suggests that some other factor aids in precipitating the asthmatic attack. Alternatively, the dose of atropine methonitrate may not have been sufficient to block reflex pathways in this patient, though previous studies suggest that a 2-mg dose does block citric-acid-aerosol-induced bronchoconstriction in humans,[12] and is the dose that produces maximum bronchodilatation.[14] In the patients tested, the aerosol insect killer did not change the non-specific bronchial hyperreactivity to histamine. Other studies have shown this to increase after exposure to ozone,[9] allergens,[10] SO_2,[11] and after upper respiratory tract infections.[12] However, in some patients in these studies, the change in bronchial reactivity occurred immediately after the provocation and had returned to baseline levels within 24 hours (even after diurnal variation is considered). Therefore, by waiting for 24 hours before remeasuring the bronchial hyperreactivity, we may have missed any change. A study of bronchial hyperreactivity after exposure to allergens reported that a significant change in PC_{20} occurred only after late asthmatic responses.[10] As far as it was possible to tell, there were no late reactions in our patients, which may account for the absence of variation.

Further work needs to be done on a larger number of patients to determine the mechanism of the reaction that occurs, and the component of the insect killer which causes the asthmatic reaction and chest tightness.

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