

Occupational asthma from biological pest control in greenhouses

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Clinical Implications

- Several species used for biological pest control in greenhouses can sensitize and cause occupational asthma and rhinitis. Allergy to insects or mites should be suspected in greenhouse workers with work-related asthma, nasal, conjunctival, and/or skin symptoms.

TO THE EDITOR:

Commercially available insects and mites are increasingly used in the biological control of whiteflies and other pests in greenhouses. We describe 2 greenhouse workers who were exposed and sensitized to the insects used for biological pest control at their workplace and who were diagnosed with occupational asthma (OA) and occupational rhinitis (OR). The cases are presented in Table I. Both patients gave their written consent.

Patient 1, a formerly healthy 29-year-old nonsmoking man had worked in greenhouses growing tomatoes since 2007. After 8.5 years, he developed, within a month, a cough, dyspnea, rhinitis, flu-like symptoms, and itchy eyes related to work. Skin swelling, itching, and redness of his middle body and face, swelling of the lips, and breathlessness occurred after a bumble bee (*Bombus Terrestris*) sting at work. The patient's employer treated the reaction with an intramuscular adrenalin injection, but no medical professionals were consulted. Because of the severity of the worker's symptoms, workplace peak expiratory flow (PEF) monitoring was not performed.

In 2016–2017, a histamine challenge at the Finnish Institute of Occupational Health (FIOH) confirmed an asthma diagnosis. Skin prick tests (SPTs) to common aeroallergens, tomato, and storage mites were negative. Serum-specific IgE to tomato, cucumber, storage mites, bumble bees, honeybees (*Apis mellifera*), wasps (*Vespula vulgaris*), and hornets (*Vespa crabro*) were normal (<0.35 kU/L). In-house extract of the parasitoid wasps *Encarsia formosa* and *Eretmocerus eremicus* (see Appendix E1 in this article's Online Repository at www.jaci-inpractice.org) was used as such in SPT and specific inhalation challenge (SIC). It caused a positive SPT reaction, and serum-specific IgE binding was detected by immunospot with the insects as such.¹ A placebo-controlled SIC with the extract was performed according to guidelines.² The patient inhaled the extract with an increasing number of inhalations through a dosimeter over a 15-minute test (explained in detail in Figure 1). An early reaction was observed in repeated challenges with a maximum forced expiratory volume in 1 second decline of 700 mL and 15.3%. Sputum eosinophils increased from 0% to 3% (Figure 1). In addition, a nasal provocation test³ with the same extract was positive.

Patient 2, a 48-year-old female smoker had worked in greenhouses growing tomatoes and cucumbers since 2006. She did not previously have asthma, allergic diseases, or atopic eczema. After 1 year, she developed work-related rhinitis, a cough, dyspnea, wheezing, and itchy eyes. Her symptoms remained constant, despite changing jobs from a tomato to a cucumber greenhouse. The patient underwent a sinus operation in 2008 because of recurring sinusitis. Reversible obstruction in spirometry confirmed asthma in 2008, and an inhaled steroid and long-acting β_2 -agonist were introduced. Erythema, itching, and swelling had been occurring on uncovered skin areas on her face, hands, and wrists since 2010.

In 2011, SPTs to aeroallergens, tomato, and cucumber at FIOH were negative. SPTs to storage mites were positive (3–5 mm) and serum-specific IgE to *Tyrophagus putrescentiae* was 0.99 kU/L; to *Lepidoglyphus destructor*, 0.96 kU/L; and to *Acarus siro*, 0.88 kU/L (normal level <0.35 kU/L). SPTs were positive to in-house extracts of a parasitoid wasp (*E. formosa*), predatory bug (*Macrolophus caliginosus*), and predatory mite (*Amblyseius swirskii*) (see Appendix E2 in this article's Online Repository at www.jaci-inpractice.org). Specific IgE was detected in the immunospot to the predatory bug *M. caliginosus* as such. SIC was performed during budesonide 800 μ g/day medication by dusting *M. caliginosus* in a vermiculite storage medium for 30 minutes on 2 separate days and by inhaling the extract of *T. putrescentiae* through a dosimeter. The SIC was negative, as was an open skin test to cucumber and *A. swirskii*. Workplace PEF monitoring was compatible with OA based on expert analyses (IL and HS) and an OASYS score of 2.60 (cutoff of 2.5; see Figure E1 in this article's Online Repository at www.jaci-inpractice.org).⁴

Above we described a patient with OA and OR to the parasitoid wasps, *E. formosa* and *E. eremicus*, confirmed by a positive SIC and nasal provocation test. The OA of patient 2 was based on sensitization to the predatory bug *M. caliginosus*, and workplace PEF monitoring, and the presumed cause of the OA was *M. caliginosus*. To our knowledge, these are the first cases of OA from commercially available insects used for pest control in greenhouses.

The presented cases showed several features typical of occupational allergy: work-related nasal, conjunctival and asthma symptoms, and bronchial hyperresponsiveness and sensitization to the insects based on both SPTs and specific IgE results. In patient 1, the SIC with the parasitoid extract showed an early positive reaction repeatedly, confirming sensitizer-induced OA. We assume that the SIC of patient 2 was negative, because we were not able to generate enough allergens in the air by dusting the predatory bug–vermiculite mixture, as it only contained a few bugs. A dosimeter challenge with extracts of pure macroorganisms may be a more efficient method for delivering these allergens than dusting. In patient 2, the use of inhaled corticosteroids during SIC may also have affected the test.

Greenhouse production is increasing in many countries with cool climates that provide fruit and vegetables during the times of the year when field-grown products are not available.⁵ Biological pest control has increased substantially in the last 10 to

TABLE I. Clinical characteristics of patients

Variable	Patient 1	Patient 2
Age, y	29	48
Sex	Male	Female
Smoking	Ex-smoker	Smoker
Pack years	1.5	25
Atopy	No	No
Duration of exposure, y		
Before respiratory symptoms	8.5	1
Medication	No	Budesonide 400 µg and formoterol 12 µg 2 doses twice a day
Spirometry		
FVC liters/% of predicted	6.29/116	4.60/142
FEV ₁ liters/% of predicted	4.65/103	3.37/121
FEV ₁ /FVC absolute %/ % of predicted	74/90	73/86
Bronchial hyperresponsiveness*	Moderate	No
FeNO, ppb	20	16
Skin prick test, mm		
Histamine hydrochloride	7	6
Negative control	0	0
Macroorganisms used in pest control		
<i>Encarsia formosa</i> + <i>Eretmocerus eremicus</i> (parasitoid wasps)†	5	4
<i>Macrolophus caliginosus</i> (predatory bug)	5	3
<i>Amblyseius swirskii</i> (predatory mite)	NT	3 and 5
Specific IgE binding (Immunospot)		
<i>E. formosa</i> + <i>E. eremicus</i>	Yes	No
<i>M. caliginosus</i>	Suggestive	Yes
<i>A. swirskii</i>	NT	No
Total IgE, kU/L	46	304
Specific inhalation challenge	Positive reaction to <i>E. formosa</i> + <i>E. eremicus</i> †	Negative to <i>M. caliginosus</i> ‡ and to <i>T. putrescentiae</i> (storage mite)
Nasal provocation test	Positive to <i>E. formosa</i> + <i>E. eremicus</i> †	NT
Workplace PEF monitoring	NT	Compatible with occupational asthma
Diagnosis	Occupational asthma Occupational rhinitis	Occupational asthma Occupational contact urticarial§

FVC, Forced ventilation capacity; FEV₁, forced expiratory volume in 1 second; FeNO, fractional exhaled nitric oxide; NT, not tested; PEF, peak expiratory flow; ppb, parts per billion.

*In histamine challenge.

†Mixture of wasps.

‡Predatory bug-vermiculite mixture contained only few bugs.

§Based on typical skin symptoms and sensitization.

20 years in Finland (personal communications, 2017). OA and allergies to several plants including tomatoes, eggplants, bell peppers, and amaryllis have been described among greenhouse workers.^{6,7} Two earlier studies have reported sensitization to predatory mites in approximately one-fifth of greenhouse workers.^{8,9} Feary et al¹⁰ also recently described OA caused by a horticultural nematode that was sprayed on plants in a water solution.

We selected the insects and the mites to the allergy and challenge tests on the basis of the species used in the patient's workplace at the time her or his symptoms occurred. Interestingly, our patients were sensitized to several macroorganisms that are used in biological pest control and belong to the taxonomical groups of wasps, predatory bugs, and mites (Table I). Patient 1 had OA from the parasitoid wasps and positive SPT to the predatory bugs. Patient 2 had positive SPTs to both parasitoid wasps, predatory bugs, and predatory mites. She was also sensitized to storage mites,

which are suggested to be present in greenhouse environments due to organic material, humidity, and suitable air temperature. The characterization of parasitoid allergens and an investigation into their potential cross-reactivity with other insect and mite allergens would clarify our clinical findings.

The insects used in biological pest control can cause OA and OR. Thus, greenhouse workers are at risk of sensitization, OA and OR, as they are exposed throughout the working day to dusts that may contain insect and mite allergens. However, the level of exposure to these allergens is unknown. Working conditions in greenhouses need to be evaluated and improved. Effective general ventilation and the use of respiratory protective equipment may be useful preventive measures. Clinicians should be aware of the sensitizing potential of the macroorganisms used in biological pest control. New asthma and rhinitis cases should be detected early to diminish or stop exposure and improve the prognosis of these patients.

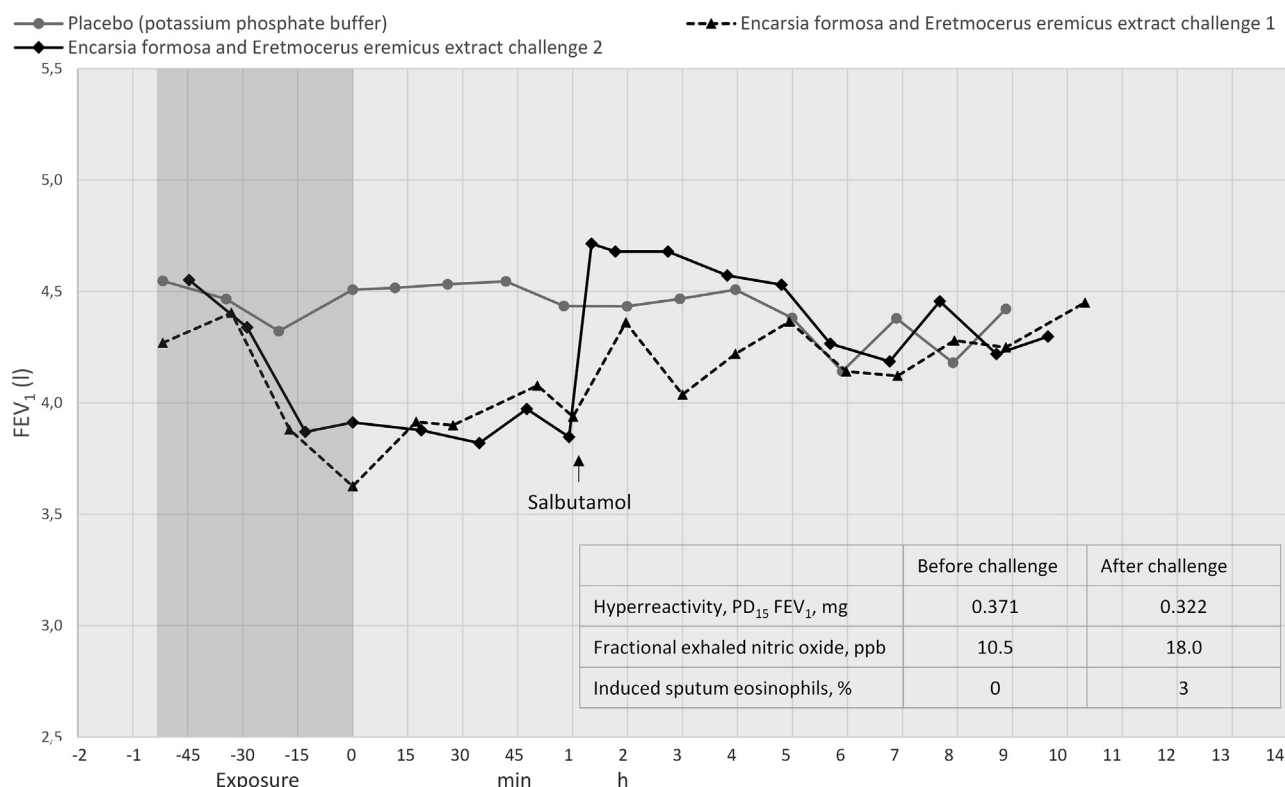


FIGURE 1. Specific inhalation challenge of patient 1, illustrating FEV₁, hyperreactivity, fractional exhaled nitric oxide (FeNO), and sputum eosinophils. In the control challenge, the patient inhaled potassium phosphate buffer through a dosimeter. In the active challenges, the patient took 1, 10, and 90 deep inhalations of the parasitoid extract through a dosimeter with an output of 5.9 mL per inhalation. FEV₁, Forced expiratory volume in 1 second.

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ONLINE REPOSITORY

APPENDIX E1

In-house extracts of the parasitoid wasps *Encarsia formosa* and *Eretmocerus eremicus* were prepared from the commercial product used at the workplace. It contained eggs from the 2 species on the carrier tape; 0.05 g of the eggs were detached from the tape and put into 2 mL of potassium phosphate buffer (0.1 M, pH 7.4), forming a 2.5% w/v solution. This solution was ultra-sonicated for 10 minutes, refrigerated overnight, sterile-filtered

the following day, and used as such in skin prick test and specific inhalation challenge.

APPENDIX E2

The *Encarsia formosa* extract was prepared as described under patient 1. *Macrolophus caliginosus* and *Amblyseius swirskii* were delivered in a vermiculite carrier, and prepared by diluting the macroorganism-vermiculite mixtures into 10% w/v potassium phosphate buffer. They were stirred for 5 hours at room temperature, refrigerated overnight, and centrifuged the following day. The supernatants were sterile-filtered and used as such in skin prick test.

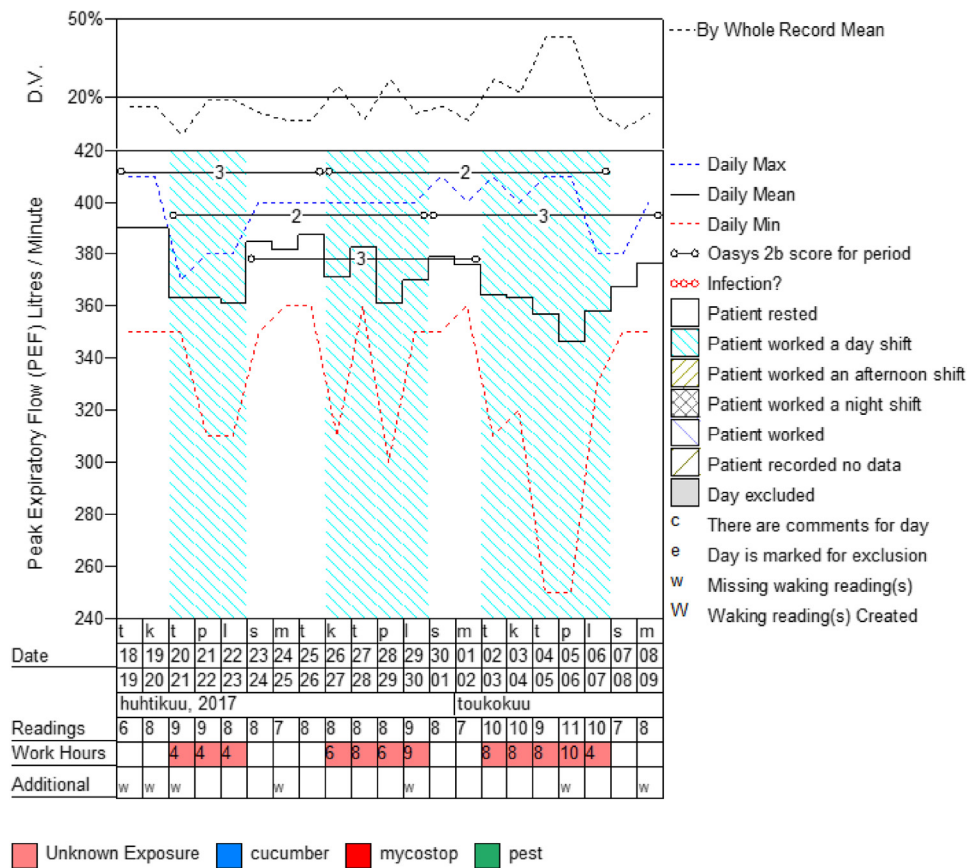
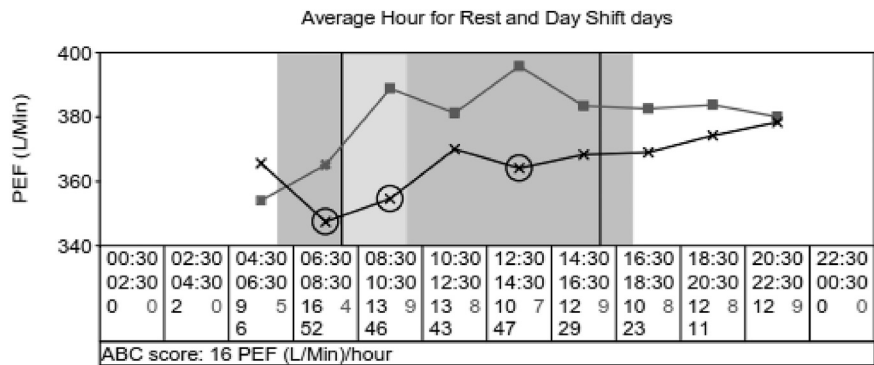
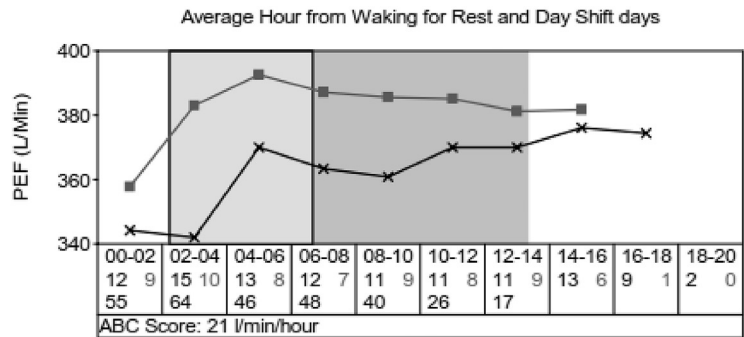


FIGURE E1. The workplace PEF monitoring of patient 2 plotted and analyzed with using the OASYS program (www.occupationalasthma.com).



Time of Day, Number of Readings And Areas (Day Shift x) (Rest ■)



Hours From Waking, Number of Readings And Areas (Day Shifts x) (Rest ■)

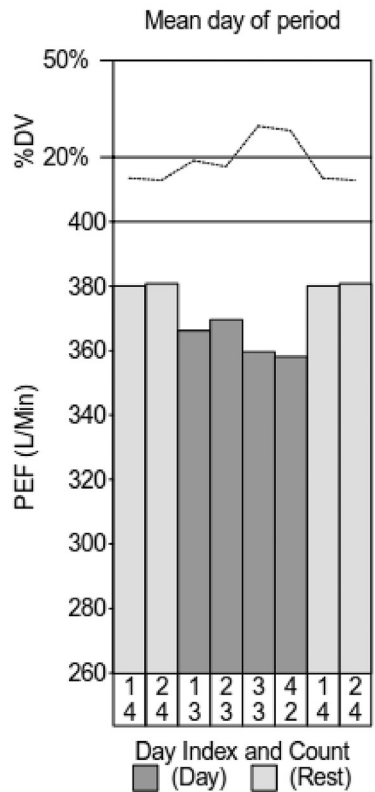


FIGURE E1. (CONTINUED).

Patient Details

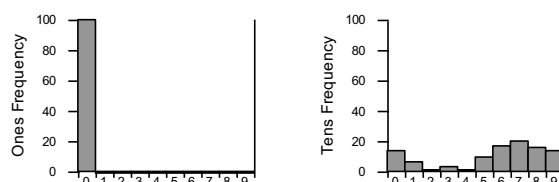
Name z-h s
Dates 18.04.2017 - 08.05.2017
Meter Mini-Wright Linear
Exposure Unknown
Workplace plant house
Jobs planting etc
Predicted 0
Treatments Inhaled Steroids
"Interpretation" Pseudo Day "Interpreted"

Quality

The record is sloping at -1 l/min per day.

There are 9 outlying readings. Outlying readings are lower than 323 l/min or higher than 419 l/min, which is the 95% confidence interval for the readings. Please check these readings.

Number Preference



Diurnal Variation

	By Whole Record Mean		
	Min	Mean	Max
Whole Record	5	18	43
Day Shift Days	5	22	43
Rest Days	8	13	16

Work Exposures

Name	Colour	Rest - Work	Number of Work Days
Unknown Exposure (in)		18 l/min	12
cucumber (in)		0 l/min	0
mycostop (in)		0 l/min	0
pest (in)		0 l/min	0

Scores

92% of workers with optimal data and a positive Oasys score will have occupational asthma.

There is no predicted PEF for this record.

Oasys score **2,60**

Rest - Work PEF Difference Absolute **18 l/min**
98% of workers with optimal data and a score ≥ 15.7 will have occupational asthma.

ABC (Area Between Curves) score Day shifts **21,09**

Timepoint Analysis Day shifts **Positive (3)**

93% of workers with analysable data and a positive timepoint score will have occupational asthma.

The website www.occupationalasthma.com can provide help interpreting this report. Click on "Help - Oasys Website" on the main menu to be taken to the website. We are happy to receive referrals, especially with the original data. Please refer to Prof Burge, Birmingham Chest Clinic, Birmingham, B3 3HX.

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