ORIGINAL ARTICLE

Post-Hire Asthma Among Insect-Rearing Workers

Eva Suarthana, MD, PhD, Angela Shen, MPH, ScD, Paul K. Henneberger, ScD, MPH, Kathleen Kreiss, MD, Norman C. Leppla, PhD, David Bueller, MA, Daniel M. Lewis, PhD, Toni A. Bledsoe, MS, Erika Janotka, MUDr, and Edward L. Petsonk, MD

Objective: To evaluate the incidence of post-hire asthma (PHA) among insect-rearing workers, defined as asthma, the symptoms of which appeared after hire at the current workplace. **Methods:** We surveyed the health of workers at three insect-rearing facilities and an associated office facility. We calculated the incidence and estimated hazard ratios for PHA. **Results:** Post-hire asthma incidence in 157 insect-rearing workers was 16.2 per 1000 person-years compared with 9.2 per 1,000 person-years in 70 office workers. Workers with predominant exposure to Lepidoptera had an incidence of 26.9 per 1000 person-years and a hazard ratio of 5.5 (95% confidence interval: 1.6 to 23.9) adjusted for sex, race, and parental asthma. In contrast, the presence of specific immunoglobulin E to Lepidoptera antigens was not associated with PHA. **Conclusion:** Insect-rearing workers had a high incidence of PHA, primarily accounted for by workplace exposure to Lepidoptera.

Exposures to insects in occupational[1–16] and domestic environments[17–20] have been associated with immunologic sensitization, as well as the development of rhinitis and asthma. A broad range of insect orders ranging from Coleoptera (beetles, weevils) to Orthoptera (grasshoppers, locusts), Trichoptera (caddis flies), Diptera (Chironomids, fish food insects, blowflies), and Dictyoptera (cockroaches) have been implicated in triggering allergy symptoms. Other surveys at insect-rearing facilities have suggested that allergic symptoms have been particularly noted by individuals who work with Lepidoptera species.[4,5,11,16]

Rearing of insects is often done for biologic control of agricultural pests.[21] During insect rearing, workers may be exposed to proteinaceous material from insects including scales, setae, wing and leg fragments, and exuviae or feces (frass).[22] Other exposures in insect-rearing facilities include bacteria, mites, fungal contaminants, insect diet components, and various chemicals.[23]

The European Community Respiratory Health Survey II estimated that 10% to 25% of all adult-onset asthma is caused by occupational exposures, which was equivalent to an annual incidence of occupational asthma of 25 to 30 cases per 100,000 workers.[24] A recent systematic analysis based on longitudinal general population surveys concluded that an estimated 16.3% of all adult-onset asthma is caused by occupational exposures.[25] Nevertheless, to the best of the authors' knowledge, no study reported the incidence of new onset of asthma among insect-rearing workers.

To further investigate factors leading to the development of occupational allergies in these unique environments, the US National Institute for Occupational Safety and Health in Morgantown, West Virginia compared the health of workers at several insect-rearing facilities with a comparison group of workers from an associated office facility. This report describes findings from the surveys and addresses the incidence of post-hire asthma (PHA) among insect-rearing workers and a comparison group of office workers.

METHODS

Participants

Participants were recruited in four facilities. Workers at three of the facilities were involved in the rearing of various insect species for agricultural pest control and research. At each of these facilities, a number of different orders of insects (class Insecta) and mites (class Arachnida) were reared, and study participants reported job exposures to a total of 53 species and 8 different orders of insects and mites. Facility A raised primarily gypsy moth, *Lymantria dispar* (L.), (order Lepidoptera: family Lymantriidae); facility B raised pink bollworm, *Pectinophora gossypiella* (Saunders), (Lepidoptera: Gelechiidae); and facility C raised several species of tropical fruit flies (Diptera: Tephritidae). Each of the insect-rearing facilities had a full respiratory protection program and instituted preventive sanitation protocols. Extensive engineering controls were in place to control exposures during routine insect contact activities.[26–28] The comparison group was recruited in a large administrative facility geographically separated from any insect rearing. Workers at this unit had no specific occupational contact with insects. We excluded from the analysis participants with incomplete data, comparison office workers who reported previous employment in insect-rearing facilities, and insect-rearing workers who indicated no current potential job exposure to insects. We also excluded participants who reported having "ever had physician-diagnosed asthma," having "ever had asthma," or having "ever had an asthmatic attack" before being hired at their current workplace.

Data Collection

Participants completed a self-administered questionnaire, reported their occupational history, received skin prick tests, and were given Mini Wright peak flow meters and log sheets. The study protocol was approved by the US National Institute for Occupational Safety and Health human subjects review board, and prior informed consent was obtained from all participants.

Questionnaires

Items on the questionnaire were derived from existing research questionnaires prepared by the British Medical Research Council, International Union Against Tuberculosis and Lung Disease, and American Thoracic Society.[29,30] The questionnaire asked about history of asthma, wheezing, or attacks of shortness of breath with wheezing. Also evaluated was the presence of respiratory symptoms

during the preceding 12 months, including attacks of shortness of breath, chest tightness, nocturnal cough, and exercise-induced dyspnea.

Exposures of Interest

Exposure was characterized in several ways: self-reported exposure to insects at work (yes/no), work tenure, and whether the predominant insect contact at work was with the order Lepidoptera (yes/no). Work tenure was calculated as time from date of hire at the facility to either asthma onset or beginning of this study, whichever was earlier. We also investigated the consequences of specific immunoglobulin E (IgE) to Lepidoptera antigens (yes/no, see later).

Specific IgE to Lepidoptera (Radioallergosorbent Test)

Bulk samples of Lepidoptera antigens from several sources at each insect-rearing facility were obtained. Extracts of bulk samples of potentially important Lepidoptera exposures at these facilities (gypsy moth, pink bollworm, and browntail moth) were dialyzed against $0.05 M \, NH_4CO_3$, lyophilized, redissolved in carbonate buffer, and coupled to cyanogens bromide–activated Sepharose beads (Pharmacia, Uppsala, Sweden) according to the manufacturer's recommendation. Coupling efficiency was estimated by determining the protein content of the extracts before and after reacting with the beads. A radioallergosorbent test (RAST) to detect IgE antibodies was developed by an initial screening of the workers' sera to identify IgE-positive and IgE-negative sera; we then used those sera to optimize the RAST assay conditions for each antigen. Results from the unexposed comparison workers were used to establish nonspecific binding values for each antigen. A RAST score above the 99th percentile of the nonspecific binding range (mean $+ 2.5 \times$ SD) was used to identify sera from exposed workers with antigen-specific IgE antibodies.

Skin Prick Test

Skin scratch testing for 18 common aeroallergens, with histamine (positive) and glycerol (negative) controls, was performed on the volar surface of the lower arms. Skin test reagents were purchased from Greer Laboratories (Lenoir, NC). The skin was cleansed with isopropyl alcohol and allowed to dry before antigen solutions were applied using a plastic disposable sterile device (DermaPic System, Greer Laboratories). The largest diameter of wheal and the diameter perpendicular to this were measured for each antigen, and the two diameters were averaged. For each antigen, the largest diameter of wheal and the diameter perpendicular to this were measured, and these two diameters averaged. Measurements were recorded at 15 and 30 minutes, and the larger of the two measurements was used in the analysis. Individuals who failed to react to histamine (≤ 3 mm mean wheal diameter) were excluded. For individual antigens, a positive reaction was defined as a mean wheal diameter of more than 5 mm. Atopy was defined as more than 5 mm mean diameter wheal to at least one of 15 allergens (ie, cat fur, dog fur, Fescue grass, Kentucky bluegrass [June grass], Red top grass, Timothy grass, Lamb Quarter weeds, English Plantain, Ragweed, Box elder, Hickory, oak, pine, Alternaria, and cockroach). Dust mites (*Dermatophagoides farinae* [Hughes], *Dermatophagoides pteronyssimus* [Trouessart]) and moth responses were excluded from the definition of atopy because many of the workers were exposed to moths at work, and immunologic cross-reactivity of various insect species and mites has also been suggested.[31,32]

Peak Flow Measurement

Workers were asked to record three blows every 2 hours while awake for 8 consecutive days. Log sheets had 12 suggested recording times for each study day, starting at 2 AM. Peak flow trials recorded between suggested recording times were assigned to the earlier time (eg, a trial recorded at 7 AM was assigned to the 6 AM recording

time). Workers were also asked to indicate metered dose inhaler use and any specified respiratory symptoms (wheezing, chest tightness, shortness of breath, coughing attacks) on the recording log sheet.

On Thursday, the first study day, workers were instructed in the correct use of peak flow meters. The next day, Friday, each participant's technique was observed by the study team and corrected if necessary. During the weekend, workers were called at home to encourage compliance. On Monday, each participant's log sheet and technique were checked during pre- and post-shift spirometry sessions to emphasize maximal effort and correct use of the meters. Although a few workers had nontraditional workday or workweek schedules, the majority worked the day shift from Monday to Friday between 6 AM and 8 PM. For participants who did not work a Monday to Friday workweek, peak flow technique and log sheets were checked in conjunction with the beginning and end of workweek spirometry sessions. Meters and logs were collected following completion of the 8-day peak flow–recording period.

An acceptable record consisted of at least 3 workdays and 2 sequential days off, with 3 or more trials consisting of 3 or more blows per trial and 8 or more hours of data per day. The largest of the three values at each recording time was used as the representative value for that time. Difference in mean peak expiratory flow (PEF) between workdays and rest days of 16 L per minute was used as the index of PEF variability to determine asthma related to work.[33]

Outcome Definition

We defined a case of asthma as an affirmative response to the following questions: "Have you ever had asthma?" or "Have you ever had an asthmatic attack?" or "Was asthma confirmed by a doctor?" We further defined PHA as asthma with age of onset equal to or greater than the age of hire at the current workplace.

Statistical Analysis

All continuous variables were dichotomized at the median value. Candidate potential confounders included personal characteristics (ie, age 32 years or older, nonwhite race, female sex), family and childhood medical history (ie, parental history of asthma, onset of nasal or skin symptoms before the age of 12 years), allergies (ie, allergies since childhood, history of hay fever, atopy based on skin tests), and cigarette smoking (ever/never).

Statistical tests were used in crude comparisons of characteristics of workers included and excluded from the analysis, as well as workers with and without insect exposures at work. We used the χ^2 statistic or Fisher exact test for categorical variables and the Wilcoxon ranked sum test for continuous variables. Hazard ratios (HRs) and the corresponding 95% confidence intervals (CIs) and P values for PHA were estimated using Cox proportional hazards analysis with work tenure as the time-varying variable. For multivariate analysis, we manually performed the backward selection method. Potential confounders with $P > 0.25$ were excluded, whereas variables with $P < 0.1$ were kept in the final model. Variables with $P \geq 0.1$ and ≤ 0.25 were kept in the final model if their removal changed covariates for occupational variables by at least 20%. $P < 0.05$ was considered statistically significant and borderline statistical significance was defined as $0.05 \leq P < 0.10$. All analyses were accomplished using SAS statistical software package version 9.2 (SAS Institute, Cary, NC).

RESULTS

Of the persons requested to participate, 5 (2.5%) of the 197 insect-rearing workers and 1 (1.1%) of the 88 office workers either declined or did not complete the initial questionnaire (Fig. 1). Thus, the 285 potential participants were reduced to 279 (participation rate 97%). In assessing the effect of insect exposures, it was necessary to exclude 25 (13%) of the insect-rearing workers who had unclear or no potential current insect exposure (eg, administrative
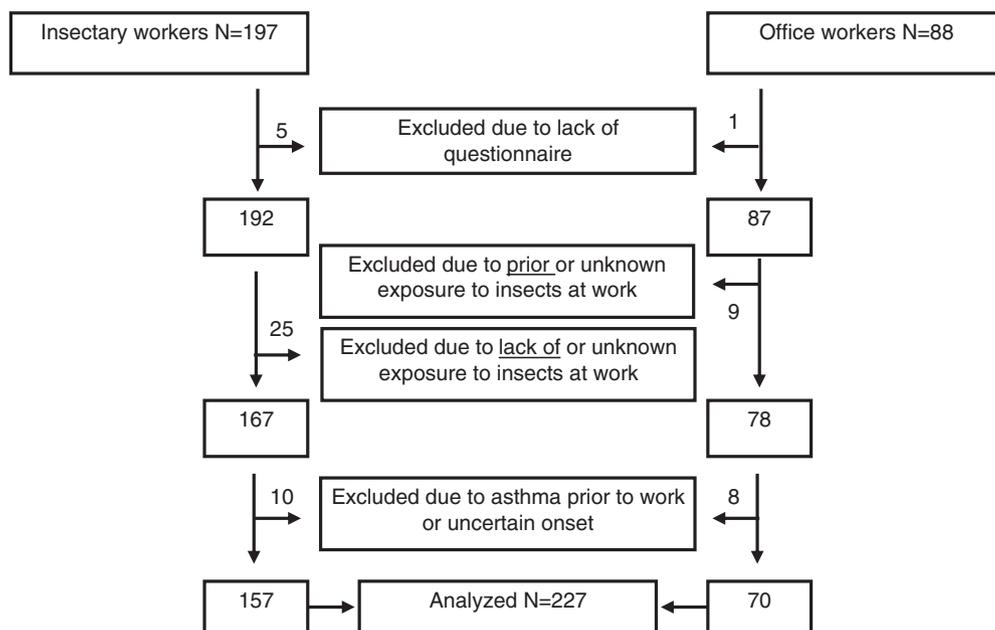
FIGURE 1. Participants from the initial surveys who were included and excluded from the analysis.

workers) and nine (10.1%) of the comparison workers who had a history of insect-rearing work. None of these 34 excluded workers had PHA. Among the remaining 245 participants, 22 (13.2%) of the 167 insect-rearing workers and 12 (15.4%) of the 78 office workers reported asthma. With regard to the 22 insect-rearing workers who reported asthma, 8 individuals developed symptoms before being hired at the facility and in 12 individuals developed symptoms after being hired, whereas for 2 individuals, the timing was uncertain. Similarly, for the 12 asthma cases in the office workers, symptom onset was before hire in 6, after hire in 4, and uncertain in 2. Thus, the percentage of participants with onset of asthma before hire was somewhat greater for the comparison group (6/78 = 7.7%) than the insect-rearing workers (8/167 = 4.8%) ($P = 0.53$). To examine the incidence of PHA, cases with either pre-hire or unknown onset were excluded from consideration. The 52 excluded participants did not differ from the 227 included participants with respect to median age, race, sex, cigarette smoking, family and medical history, and skin prick test results (Table 1). A history of allergies since childhood was somewhat more common among the excluded participants. Of the 227 included participants, 158 had RAST to Lepidoptera and 44 (28%) of them had positive results, whereas none of the excluded participants had RAST results.

   As shown in Table 2, insect-rearing workers were very similar to the office workers with respect to several characteristics, including age, race, smoking habit, as well as sensitization to dust mite and moth. However, from comparisons that were statistically significant or borderline significant, office workers had longer work tenure and higher proportions of women, parental asthma, nasal symptoms, allergies since childhood, and atopy compared with insect-rearing workers.

   Peak expiratory flow data were available for 140 insect-rearing and 68 office workers and were acceptable for 132 insect-rearing and 62 office workers. The two groups showed comparable difference in mean PEF between rest and workdays (Table 2). Acceptable PEF data were available in 13 of 16 workers with PHA. Two of nine (22%) insect-rearing workers with PHA had a rest–work PEF difference of 16 L per minute or more, whereas none of the office workers with PHA had this PEF index of asthma related to work (data not shown).

   Post-hire asthma incidence in insect-rearing workers was 16.2 per 1000 person-years (pyr), whereas the incidence in office workers was 9.2 per 1000 pyr (Table 3). Workers with predominant exposure to Lepidoptera had an incidence of 26.9 per 1000 pyr, whereas workers exposed to other insects had an incidence of 3 per 1000 pyr. Unadjusted analysis revealed no significant association between PHA and various characteristics, although PHA incidence tended to be greater with exposure to Lepidoptera (HR = 2.7; 95% CI: 0.9 to 9.9) and reduced with exposure to other orders (eg, Diptera [HR = 0.3; 95% CI: 0.02 to 2.0]).

   The first PHA multivariate model included sex, race, parental asthma, and exposures to insects at work (Table 4) and demonstrated that insect-rearing workers had an elevated incidence in comparison with office workers (HR = 4.5; 95% CI: 1.2 to 21.3). In the second model, we evaluated the association of PHA and type of insect exposures, while adjusting for sex, race, and parental asthma (Table 5). The second model revealed that workers with predominant exposures to the Lepidoptera order of insects had an elevated HR of 5.5 (95% CI: 1.6 to 23.9), whereas exposure to other orders of insects yielded a nonsignificant reduction in PHA incidence (HR = 0.7; 95% CI: 0.03 to 6.3). In addition, we evaluated interaction between the predominant insect exposure and tenure. The estimated HRs for predominant exposure to the various insect orders did not change with increasing work tenure (data not shown). A third PHA multivariate model evaluated the combined effects of Lepidoptera exposure and a positive RAST test (yes or no, reflecting the presence of IgE to moth antigens collected from the insect-rearing facilities, Table 6). The comparison group for the exposure categories comprised individuals with negative RAST tests and no workplace Lepidoptera exposure. Complete RAST tests were available for only 158 persons, reducing the statistical power. As seen with the unadjusted analyses (Table 3), Lepidoptera exposure had a much stronger association with PHA than positive RAST status. No PHA cases were identified among individuals with a positive RAST test in the absence of Lepidoptera exposure. In contrast, among Lepidoptera-exposed insectary workers, the HR was high (HR = 5.5; 95% CI: 1.3 to 23) when the RAST test was positive and decreased only slightly among exposed persons with negative RASTs (HR = 4.1; 95% CI: 0.9 to 19).

DISCUSSION

   This is the first study demonstrating the excess incidence of PHA in insect-rearing workers, especially in workers with

TABLE 1. Comparison of Survey Participants Included and Excluded From Analyses

Characteristics	Participants Included (n = 227)	Participants Excluded (n = 52)	P
Age at hire, yr, median (minimum–maximum)*	32.0 (17–66)	34.0 (21–55)	0.17
Race, white, % (n)	82 (185)	77 (40)	0.45
Sex, women, % (n)†	42 (96)	37 (19)	0.51
Smoke cigarettes, % (n)			
Current	27 (61)	27 (14)	0.96
Former	22 (50)	24 (12)	
Never	51 (116)	49 (25)	
Family and medical history, % (n)			
Parental asthma‡	7 (16)	13 (6)	0.24
Nasal symptoms, onset <12 yr of age	13 (29)	15 (8)	0.62
Skin symptoms, onset <12 yr of age§	1 (2)	4 (2)	0.15
Allergies, % (n)			
Allergies since childhood	55 (125)	69 (36)	0.06
Ever hay fever	26 (59)	35 (18)	0.21
Skin prick test, % (n)‖			
15 common allergens (atopy)	66 (143)	71 (32)	0.52
Dust mite allergens	33 (72)	44 (20)	0.16
Moth allergens	15 (32)	16 (7)	0.90
Any common allergens	70 (152)	76 (34)	0.48
Total immunoglobulin E level ≥ 100 kU/L, % (n)¶	35 (61)	44 (16)	0.28

*Nine of the excluded participants had not reported their age at hire.

†One of the excluded participants had not reported his/her sex.

‡Eleven of the included participants and six of the excluded participants did not answer the question about parental asthma.

§One of the included participants and three of the excluded participants did not answer the question about skin symptoms.

‖Eleven of the included participants and seven of the excluded participants did not have skin test results for determining atopy. The 15 common allergens included cat fur, dog fur, Fescue grass, Kentucky blue (June grass), Red top grass, Timothy grass, Lamb Quarter weed, English Plantain, Ragweed, Box elder, Hickory, oak, pine, Alternaria, and cockroach. Dust mite allergens included *D. farinae* and *D. pteronyssimus*. All 39 subjects reacting to moth allergens also reacted to at least 1 of the 15 common allergens.

¶Fifty-two of the included participants and 16 of the excluded participants did not have results for total immunoglobulin E level.

predominant exposure to Lepidoptera. We found that the annual PHA incidence was 16.2/1000 workers in insect-rearing facilities and 9.2 in office workers. From the epidemiologic follow-up survey of the First National Health and Nutrition Examination Survey (NHANES I), the estimated incidence of new-onset asthma among adults was 2.1 per 1000 pyr.[34] The incidence difference between the NHANES and our study may be explained at least in part by different asthma definitions. The NHANES used "ever had physician diagnosed asthma" question, whereas we used a more inclusive asthma definition by including "ever had physician diagnosed asthma" or having "ever had asthma" or having "ever had an asthmatic attack." If we restricted our definition to "ever had physician diagnosed asthma," the incidence of PHA would be 12.2 per 1000 pyr among insectary workers, but unchanged among the office workers.

When stratified by exposure to various insect orders, it seemed that workers with predominant exposure to the Lepidoptera order had a remarkably high incidence of PHA (26.9 per 1000 pyr). In contrast, the insect-rearing workers with predominant exposure to non-Lepidoptera had an incidence rate for PHA of only 3 per 1000 pyr. From multivariate regression with office workers as the common reference group, Lepidoptera workers had an elevated HR and non-Lepidoptera workers had an HR close to 1 (Table 5). A positive RAST (indicating specific IgE to Lepidoptera antigens present in these insect-rearing facilities) seemed to be less of an explanatory factor for asthma development than the workplace exposure to Lepidoptera.

Although there have been numerous case reports of reactions to insect-derived materials, there have been few formal studies

of occupational exposures to Lepidoptera. Etkind et al[5] studied 17 individuals exposed to gypsy moth caterpillar and found that 9 of the 10 workers with occupational allergy symptoms showed a reaction on skin scratch testing with specific moth extracts; however, 5 of the 7 exposed workers without allergy symptoms also reacted. Etkind and coworkers observed fewer reactions using commercial moth extracts than the specific workplace-derived antigens, similar to our results. Bauer and Patnode[11] performed a mail survey of workers in 98 insect-rearing facilities. About 25% of employees in these facilities reported skin and/or respiratory tract symptoms attributed to work exposures, and Lepidoptera were the most commonly implicated insects. In a study of 53 female silk industry workers in Sri Lanka, more than half reported at least 1 respiratory symptom and 18 were identified with PHA.[16] Four of the 18 PHA cases showed that PEF declines across a work shift more than 15%. Immunologic studies were not reported. A number of Diptera species have been reported to be allergenic, including fruit flies (Drosophilidae), screwworm flies, *Cochliomyia hominivorax* (Coquerel), other blow flies (Caliphoridae), and midges (Chironomidae).[2,7,8,12,22] Spieksma et al[15] reported the presence of respiratory symptoms in one third of laboratory workers exposed to the fruit fly, *Drosophila melanogaster* (Meigen). Baur and Liebers[2] reported increased risks of sensitization and of bronchial asthma in subjects exposed to midges. Another study among fish-food workers exposed to Chi t1 antigens showed that asthmatic workers had the highest antigen levels and both symptoms and sensitizations were associated with the degree of exposure.[8] The unremarkable incidence of PHA seen in this study among

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TABLE 2. Comparison of Insect-Rearing and Office Workers for Demographic and Other Factors

Characteristics	Insect-Rearing Workers ($n = 157$)	Office Workers ($n = 70$)	P
Demographic characteristics			
Age at hire, yr, median (minimum–maximum)	31 (17–66)	34 (17–61)	0.30
Age ≥ 32 yr, % (n)	50 (78)	59 (41)	0.22
Race, white, % (n)	82 (128)	81 (56)	0.95
Sex, women, % (n)	31 (48)	69 (48)	<0.001
Smoke cigarettes, % (n)			
Current	26 (18)	27 (43)	0.14
Former	30 (21)	19 (29)	
Never	44 (31)	54 (85)	
Family and medical history, % (n)			
Parental asthma*	3 (5)	16 (11)	<0.001
Nasal symptoms, onset <12 yr of age	10 (16)	16 (13)	0.08
Skin symptoms, onset <12 yr of age†	1 (2)	0 (0)	1.0
Allergies, % (n)			
Allergies since childhood	50 (78)	67 (47)	0.02
Ever hay fever	27 (42)	24 (17)	0.70
Skin prick test, % (n)‡			
15 common allergens (atopy)	62 (91)	74 (52)	0.08
Dust mite allergens	36 (52)	29 (20)	0.30
Moth allergens	13 (19)	19 (13)	0.28
Any allergens	66 (97)	79 (55)	0.07
Sensitization to Lepidoptera, % (n)§	33 (35)	17 (9)	0.04
Total immunoglobulin E level $\geq$ 100 kU/L, % (n)¶	40 (48)	24 (13)	0.04
Work tenure, yr, median (minimum–maximum)	2.3 (0.1–29.7)	3.5 (0.1–28.5)	0.04
Work tenure ≥ 3 yr, % (n)	46 (72)	59 (41)	0.08
PEF rest–work difference, in L/min, median (minimum–maximum)‖	−3.0 (−44.0—57.0)	−1.1 (−39.8– 37.2)	0.49
PEF rest–work difference ≥ 16 L/min, % (n)‖	6 (8)	5 (3)	0.73

*Nine insect-rearing workers and two office workers did not answer the question about parental asthma.
†One of the insect-rearing workers did not answer the question about skin symptoms.
‡Eleven of the insect-rearing workers did not have skin prick test results.
§Fifty-one of the insectary rearing and 18 of the office workers did not have radioallergosorbent test results for sensitization to Lepidoptera.
¶Thirty-seven of the insectary rearing and 15 of the office workers did not have results for total IgE level.
‖Seventeen insect-rearing workers and two office workers did not have PEF data. Of those who had data, adequate PEF were available in 132 insect-rearing and 62 office workers.
PEF indicates peak expiratory flow.

persons who worked with Diptera species might be explained by the fact that Diptera do not have scales. Despite rigorous implementation of engineering controls at the facilities, it is particularly difficult to prevent exposure to the wing and body scales of adult Lepidoptera. This might explain why workers who reared Lepidoptera had a significantly higher risk of occupational allergic diseases.

Anees[33] suggested that when analyzing serial PEF, the index that best identified workers with occupational asthma was a 16-L per minute difference in mean PEF between rest and workdays. In this study, 3 of 12 insect-rearing workers with PHA had this PEF index, whereas none of the four office workers with PHA had it. Although the numbers were small, the PEF findings tend to show that most of insect-rearing workers who report new onset of asthma did not demonstrate airflow changes related to their workplace exposures. Despite apparent excess of PHA, this PEF index appeared to be less sensitive in this study than in the original study (sensitivity 22% vs 70%), which may in part be explained by the shorter observation period of only 8 days in this study and at least 3 weeks in the original study.[35]

Consistent with another study of risk factors for asthma,[36] both of the multivariate models suggested increased PHA among workers with a history of parental asthma. Nevertheless, in contrast to a number of previous investigations, in this study neither allergies nor atopy, as evidenced by skin wheal and flare reactions to common aeroallergens, was significantly associated with asthma onset while working at an insect-rearing facility. This lack of association may be due to a healthy worker effect, in which individuals who *a priori* have increased risk of developing occupational allergies often choose to work in jobs without aeroallergen exposures or promptly leave the exposed workplace when symptoms develop.[37] In this study, a healthy worker effect is suggested by the lower proportions of allergies and atopy in insect-rearing workers than in office workers. Also, consistent with the expectation that people with asthma would avoid seeking work with allergen exposures, the percentage of participants with pre-hire asthma was somewhat greater for the comparison office workers than the insect-rearing workers. Moreover, a substudy at facilities A and B that mainly breed Lepidoptera showed that workers with the highest nasal fluid insect fragment counts, which reflected high acute respiratory exposures, did not report any respiratory symptoms.[38]

For certain high-molecular-weight antigens, the quantitative level of workplace allergen exposure has been related to the prevalence of sensitization, airway hyperresponsiveness, and allergy symptoms.[39] Even without occupational exposures, a proportion of allergic patients can demonstrate evidence of specific serologic

TABLE 3. Unadjusted Associations Between Post-Hire Asthma and Various Characteristics

Characteristics	N	PHA, n	PHA incidence*	Hazard Ratios (95% CI)†	P
Demographic characteristics					
Age at hire					
≥32 yrs	119	6	11.8	0.7 (0.2–2.0)	0.54
<32 yrs	108	10	15.0		
Race					
White	185	15	15.2	3.0 (0.6–54.3)	0.29
Nonwhite	42	1‡	5.3		
Sex					
Women	96	9	19.0	1.9 (0.7–5.3)	0.21
Men	131	7	10.0		
Smoke cigarettes					
Current	61	2	6.7	0.6 (0.1–2.4)	0.49
Former	50	7	24.1	1.9 (0.7–5.6)	0.23
Never	116	7	11.9		
Family and medical history					
Parental asthma					
Present	16	3	30.9	2.6 (0.6–8.2)	0.15
Absent	200	13	12.7		
Nasal symptoms, onset <12 years of age§					
Present	29	0	0	0	0.23
Absent	198	16	14.7		
Skin symptoms, onset <12 years of age§					
Present	2	0	0	0	1.0
Absent	222	14	13.2		
Allergies					
Allergies since childhood					
Present	125	8	13.4	1.0 (0.4–2.7)	0.96
Absent	102	8	13.8		
Hay fever					
Ever	59	3	10.1	0.8 (0.2–2.4)	0.66
Never	168	13	14.8		
Skin prick test					
15 common allergens (atopy)					
Present	143	12	16.1	1.6 (0.6–5.8)	0.40
Absent	73	4	9.7		
Dust mite allergens					
Present	72	6	18.3	1.4 (0.5–3.8)	0.52
Absent	144	10	12.1		
Moth allergens					
Present	32	4	21.0	1.7 (0.5–5.0)	0.36
Absent	184	12	12.4		
Any allergens					
Present	152	12	15.3	1.4 (0.5–4.6)	0.60
Absent	64	4	10.8		
Sensitization to Lepidoptera					
Present	44	5	17.5	1.7 (0.5–5.4)	0.37
Absent	114	7	10.9		
Total IgE level ≥100 kU/L					
Present	61	7	23.4	2.6 (0.8–8.3)	0.10
Absent	114	5	8.0		
				(Continued)	

TABLE 3. *(Continued)*

Characteristics	N	PHA, *n*	PHA incidence*	Hazard Ratios (95% CI)†	P
Insect exposures at work					
Present	157	12	16.2	1.6 (0.6–5.8)	0.40
Absent	70	4	9.2		
Predominant insect exposure					
Lepidoptera	86	11	26.9	2.7 (0.9–9.9)	0.09
Non-Lepidoptera	70	1‡	3.0	0.3 (0.02–2.0)	0.27
Absent	70	4	9.2		

*PHA incidence per 1000 person-years
†Hazard ratios and the corresponding 95% CIs and *P* values were estimated using Cox proportional hazards analysis.
‡Incidence based on only one case and associated hazard ratio should be interpreted cautiously.
§The proportions of PHA between workers with and without nasal or skin symptoms were compared with χ^2 test or Fisher exact test.
PHA indicates post-hire asthma; CI, confidence interval.

TABLE 4. Multivariate Model for Post-Hire Asthma Including Sex, Race, Parental Asthma, and Exposures to Insects at Work

Predictors	Hazard Ratios	95% CI	P
Sex, women	3.0	1.0–9.3	0.054
Race, white	4.0	0.8–74.4	0.183
Parental asthma	3.6	0.7–13.9	0.087
Exposed to insects at work	4.5	1.2–21.3	0.040

CI indicates confidence interval.

TABLE 5. Multivariate Model for Post-Hire Asthma Including Sex, Race, Parental Asthma, and Predominant Exposures to Lepidoptera

Predictors	Hazard Ratios	95% CI	P
Sex, women	2.0	0.7–6.3	0.209
Race, white	4.5	0.9–82.6	0.151
Parental asthma	3.3	0.7–12.0	0.093
Predominant exposure to non-Lepidoptera	0.7	0.03–6.3	0.764
Predominant exposure to Lepidoptera	5.5	1.6–23.9	0.013

CI indicates confidence interval.

TABLE 6. Multivariate Model for Post-Hire Asthma Including Sex, Race, Specific Lepidoptera RAST Results, and Predominant Exposures to Lepidoptera (*N* = 158)*

Predictors	Hazard Ratios	95% CI	P
Sex, women	2.9	0.9–9.2	0.08
Race, white	4.2	0.5–34	0.17
No Lepidoptera exposure, positive RAST	†		
Lepidoptera exposure, negative RAST	4.1	0.9–19	0.07
Lepidoptera exposure, positive RAST	5.5	1.3–23	0.02

*Workers with no Lepidoptera exposures and a negative RAST test comprise the comparison group for hazard ratios.
†Hazard ratio is undefined in this group because there were no post-hire asthma cases.
CI indicates confidence interval; RAST, radioallergosorbent test.

responses to mites and moths due to immunologic cross-reactivity or nonoccupational sensitization to various insect species and mites.[31,32] In this study, dust mite and moth responses were excluded from the definition of atopy. Nevertheless, additional analysis showed that individuals who worked in insect-rearing facilities were more likely to show skin test reactivity to commercial extracts from the American house-dust mite *D. farinae* (Hughes) but not from the European house-dust mite *D. pteronyssimus* (Trouessart) (Arachnida: Acari: Pyroglyphidae) or moths (data not shown). Increased exposure to the specific dust mite or to a cross-reacting antigen in the workplace may explain this finding. Nevertheless, no relationship was observed between *D. farinae* reactivity and PHA.

Our study has a number of limitations. The cross-sectional design of participant recruitment introduced the bias of not including people who began employment but then left prior to the beginning of the study because of work-related health problems. Although we analyzed the exposure response in a retrospective cohort manner, an inception cohort that followed workers prospectively from hire would provide a more complete account of the impact of occupational exposures. The characterization of insect exposure was rather crude, limited to identification of predominant insect order and species. Also, asthma-related exposures, such as dampness, were not investigated in the office building of the comparison participants, which, if present, might have contributed to asthma onset and minimized the contrast in PHA prevalence with the insect-rearing workers.

We used a broad PHA definition to have a sufficient number of cases (ie, *n* = 16). If we restricted PHA definition to physician-diagnosed asthma, we would lose three cases. If we added the condition of having a PEF rest–work difference of more than 16 L per minute to the PHA definition, we would lose five cases. If we added the condition that asthma symptoms worsened when returned to work or improved when away from work, we would lose 10 cases. We used self-reports of asthma, which tend to have reasonable specificity but low sensitivity, so it is possible that some cases of asthma were missed.[40] Given our intent to study asthma that could have a work-related onset, we appropriately limited our attention to cases that clearly occurred after hire.

The results of this study have implications for preventive strategies in facilities with insect exposures. The findings from this study and others suggest that work with Lepidoptera species (moths

and butterflies) results in an increased risk of PHA. Facilities that rear these species should have particular precautions to reduce workplace exposures through careful design of ventilation systems, through other engineering exposure controls such as confinement of adult insects, and through housekeeping and maintenance.[26,41] There is evidence that some housekeeping methods may reduce the risk to workers in these facilities. Work-related symptoms of allergy were not reported in areas of one Lepidoptera-rearing facility that was specially constructed with waterproof concrete blocks so that all surfaces could be thoroughly cleaned with a wash down method. In addition, a wet-vacuum method was applied to remove the washings.[4,11] There is also evidence that medical monitoring and targeted intervention can reduce the onset and severity of occupational asthma[42] and should be considered for workers with occupational exposure to insects. Nevertheless, preplacement screening for atopy is unlikely to be effective in reducing the prevalence of asthma among workers exposed to insects and is not recommended.[42]

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