

Intranasal air sampling in homes: Relationships among reservoir allergen concentrations and asthma severity

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Background: The relationship among inhaled allergen exposure, sensitization, and asthma severity is unknown. **Objectives:** To investigate the relationship among personal allergen exposure, reservoir dust allergen concentrations, and physiological measures of asthma severity; to examine the numbers of particles inspired that react with autologous IgE and IgG₄.

Methods: A total of 117 patients with asthma wore 5 nasal air samplers (NASs) at home: 1 each for exposure to mite, cat and dog allergens, NAS-IgE, and NAS-IgG₄. NASs were processed by HALOgen assay for allergen measurement and incubated with autologous serum for detection of NAS-IgE and NAS-IgG₄. Reservoir allergen concentrations were measured by ELISA. Subjects' asthma severity was ascertained by measurement of lung function, exhaled nitric oxide, and nonspecific bronchial reactivity to histamine.

Results: Nasal air sampler counts correlated with reservoir concentrations for cat ($r = 0.31$; $P = .001$) and dog ($r = 0.20$; $P = .03$) but not mite allergen ($r = 0.001$; $P = 1.0$). There was no significant relationship between sensitization with exposure measured by NAS to any allergen and PD₂₀FEV₁ ($F[3,60] = 1.60$; $P = .20$); however, sensitization with exposure in dust reservoirs had significant effects on PD₂₀FEV₁ for any allergen ($F[3,59] = 3.12$; $P = .03$), cat ($F[3,59] = 3.77$; $P = .01$), and mite ($F[3,59] = 2.78$; $P = .05$), but not dog ($F[3,59] = 1.06$; $P = .37$). We repeated the analysis with separate variables for sensitization and exposure, controlling for the confounders; sensitization but not exposure conferred lower PD₂₀FEV₁ values. However, increasing cat allergen exposure was associated with improving bronchial reactivity in not cat-sensitized patients. NAS-IgE and NAS-IgG₄ counts bore no relationship to any measure of asthma severity.

Conclusion: Nasal air samplers confer no advantage over reservoir dust analysis for studies of asthma severity.

Clinical implications: In common with other measures of exposure, single nasal air samples do not provide a useful

measure of home allergen exposure for the individual patient with allergic asthma. (*J Allergy Clin Immunol* 2006;117:649-55.)

Key words: Allergen exposure, sensitization, nasal air sampling, asthma severity, bronchial reactivity

Experimental allergen challenge in sensitized individuals results in early and then late decline in lung function and an increase in airway reactivity and exhaled nitric oxide (eNO), which are associated with a persisting influx of eosinophils and T lymphocytes into small airways.^{1,2} However, evaluating the effect of real-life allergen exposure on asthma severity is more challenging.

Spirometry, bronchial reactivity (BR), and eNO concentrations reflect different aspects of lung physiology. Increased BR is associated with airways remodeling^{3,4} but has not been invariably associated with airways inflammation.^{5,6} Recent animal studies demonstrated that airways inflammation can be induced by brief allergen challenge, whereas chronic allergen exposure is required for the persistence of BR and the development of airway remodeling.⁷⁻⁹ In human studies, no single measure of asthma severity has best characterized the relationship between allergen exposure and disease activity. Sensitized patients with asthma exposed to high allergen levels in their homes have reduced lung function;¹⁰ BR and eNO appear increased in atopic patients with asthma exposed to high levels of sensitizing allergen.¹⁰⁻¹² eNO increases in patients with asthma with pollen allergy during the pollen season and falls after the season is over,¹³ whereas allergen avoidance in mite-sensitized patients with asthma at high altitude results in lower eNO.¹⁴ High allergen exposure in sensitized patients with asthma increases the risk of hospital admission.^{15,16}

Most previous studies used reservoir dust allergen concentrations as an index of personal exposure, yet they provide only an indirect measure of inhaled allergen. Personal air samplers may provide a more direct measure^{17,18} but are too cumbersome for use in large studies. The nasal air sampler (NAS) allows a direct measure of personal allergen exposure.¹⁹ This device contains an adhesive membrane for collecting inspired particles (90% > 5 μm)²⁰ and is able to detect allergens using short sampling periods.^{21,22}

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Abbreviations used

BR:	Bronchial reactivity
eNO:	Exhaled nitric oxide
GM:	Geometric mean
NAS:	Nasal air sampler
NS/E:	Not sensitized but exposed to any study allergens
NS/NE:	Not sensitized and not exposed to any study allergens
S/E:	Sensitized and exposed to 1 or more specific allergens
S/NE:	Sensitized but not exposed to any study allergens
UK:	United Kingdom

We hypothesized that (1) allergen sensitization with high personal allergen exposure increases asthma severity, and (2) the number of inspired particles reacting with autologous IgE is positively related to asthma severity. We also examined the relationship between personal allergen exposure and reservoir dust allergen concentrations and measured the numbers of inspired particles that react with autologous IgG₄.

METHODS

Subjects meeting the following inclusion criteria were recruited from our clinical trials database and outpatient department: physician-diagnosed asthma, asthma symptoms in the past 12 months, using asthma medication, and no asthma exacerbation or chest infection in the 4 weeks before attendance. Subjects signed a written consent, and the study was approved by the local research ethics committee. Before attendance, subjects had avoided short-acting bronchodilators (6 hours), long-acting bronchodilators and theophyllines (24 hours), and antihistamines (48 hours).

Exhaled NO was determined by using a chemiluminescence analyser (LR 2000; Logan Research, Rochester, United Kingdom [UK]) as described previously.¹⁰

Spirometry was measured by using a MicroLab 3000 spirometer (MicroMedical, Rochester, UK). The best of 3 technically acceptable FEV₁ efforts was recorded.

Histamine challenge test was performed if the subject's FEV₁ was $\geq 60\%$ predicted. A modified Yan technique was used to obtain a cumulative PD₂₀FEV₁ (Koko DigiDoser dosimeter; PDS Research, Louisville, Colo; "646" nebulizer pots; Devilbiss, Somerset, Pa).^{10,23} In subjects who did not reach a 20% fall in FEV₁ after the challenge, a PD₂₀ of 12 mg was entered as the result (1 doubling dose above the final cumulative dose).

Allergic sensitization was ascertained by measuring specific serum IgE (mite, cat, dog; ImmunoCAP; Pharmacia, Uppsala, Sweden). We defined sensitization as specific IgE > 0.35 kU/L.

Nasal air sampling

Subjects collected 5 NAS measurements. One sampler was worn in bed on retiring for the evening. A period of 15 minutes was allowed for bed disturbance to settle, and the sampler was then worn for 30 minutes. Four samplers were worn in the living room for 15 minutes each on separate occasions during sedentary activity. Subjects were asked to nose-breathe throughout the sampling period. The majority (80%) of individuals performed nasal air sampling within 4 weeks of issue.

The 30-minute sample was incubated with anti-Der p 1 mAb. The four 15-minute samples were randomly allocated for the processing with the following primary antibodies: anti-Fel d 1, anti-Can f 1, and autologous serum with either antihuman IgE or antihuman IgG₄ as the secondary antibody.

For the aeroallergens, nasal air samples were processed by using the HALOgen (Inhalix, Sydney, Australia) protocol.²⁴ Briefly, pairs of adhesive tapes from nasal air samplers were laminated onto a protein-binding membrane and immunostained. Positive control tapes were provided in the HALOgen kits; negative control tapes were made by laminating unexposed adhesive tape in the laboratory.

Two nasal air samples were processed for reaction with autologous serum and immunostained for IgE (NAS-IgE) or IgG₄ (NAS-IgG₄). Samples were laminated onto protein-binding membrane taken from the HALOgen kits, prewet in 80% methanol for no longer than 60 seconds, washed in distilled water, and allowed to elute and block in blocking buffer (milk powder 5%/PBS/Tween-20 0.05%) overnight at 4°C. Samples were washed, incubated with neat autologous sera, washed, incubated with either biotinylated goat antihuman IgE (#16-10-04; KPL; Gaithersburg, Md) or biotinylated antihuman IgG₄ (B-3648; Sigma-Aldrich, Gillingham, UK), washed, incubated with avidin-alkaline phosphatase conjugate (Sigma-Aldrich, E2636), washed, and developed in bromo-4-chloro-3-indolyl phosphate/nitro blue tetrazolium (Sigma-Aldrich, B1911). Washes were performed 3 times for 10 minutes each in PBS/Tween-20 0.05%. Antibody incubations were for 2 hours at room temperature. Secondary and tertiary antibodies were used at 1/500 concentration in blocking buffer. An overnight soak in wash buffer at 4°C between the anti-IgE/anti-IgG₄ and avidin-alkaline phosphatase conjugate steps reduced background staining.

Samples were coded and analyzed blind. Each allergen-bearing particle appeared as a halo of color surrounding an inspired particle. Particles were counted 3 times by using light microscopy ($\times 40$). The particle units are represented by counts, where 1 count is 1 observed allergen-bearing particle.

Reservoir allergen concentration

Dust samples were collected by vacuuming 1 m² of living room carpet and mattress for 2 minutes.²⁵⁻²⁷ Allergen was extracted, stored, and measured by ELISA as previously described.²⁵⁻²⁷

Statistical methods

Statistical analysis was performed by using SPSS 11.0 (SPSS Inc, Chicago, Ill). Reservoir dust concentrations, PD₂₀FEV₁, and eNO were log-normalized; summary data are presented as geometric mean (GM) with 95% CIs. NAS count summary data are presented as medians and ranges. Correlations between untransformed data were assessed by using the Spearman rank test. The relationships among sensitization, exposure, and asthma severity (FEV₁% predicted, eNO, and PD₂₀FEV₁) were assessed by ANOVA in 2 different ways.

Combined effects of sensitization with exposure. We created 4 categorical variables combining sensitization with exposure (not sensitized, not exposed to any allergen [NS/NE]; sensitized but not exposed [S/NE]; not sensitized but exposed [NS/E]; sensitized and exposed [S/E]). A planned contrast compared the S/E group with the mean of the other 3 groups, testing the hypothesis that an individual who is both sensitized and exposed to an allergen will have more severe asthma than an individual in any of the other 3 groups. The analysis was performed for any allergen and then repeated for each individual allergen. High exposure was defined as Der p 1 ≥ 2 $\mu\text{g/g}$, Fel d 1 and Can f 1 ≥ 10 $\mu\text{g/g}$.^{28,29} For halo counts, subjects were arbitrarily considered exposed to an allergen if their counts were in the uppermost tertile.

Separate effects of sensitization, exposure, and their interaction. We used separate variables for sensitization (sensitized vs not), exposure (exposed vs not), and the interaction between the 2, adjusting for the potential confounding variables (age, sex, smoking, and the use of inhaled corticosteroids).

Count data for NAS-IgE and NAS-IgG₄ staining were compared with the degree of sensitization and exposure (NAS) for each allergen in turn. Because count data for NAS-IgE and NAS-IgG₄ could not be square-root normalized, ordinal regression was used: NAS-IgE data were categorized into tertiles (lower, middle, upper) and NAS-IgG₄ data into quartiles (lowest, lower, upper, highest); covariates for sensitization (the specific IgE titer for the allergen of interest) and allergen exposure (the square root-transformed NAS counts for that allergen³⁰) were used. The analysis was performed for each aeroallergen.

Relationships between NAS-IgE or NAS-IgG₄ and asthma severity were explored by Kruskal-Wallis test: FEV₁ and PD₂₀FEV₁ data were categorized into groups of severity by convention, and raw count data for NAS-IgE or NAS-IgG₄ were used in the analysis.

RESULTS

A total of 117 patients participated in the study; complete nasal air sampler data were available on 114. The characteristics of the study population are shown in Table I.

Reservoir dust allergen concentrations and HALO counts

Pet owners had significantly higher exposure to pet allergens, both in reservoir dust and by NAS (Table II). However, the fold difference between these groups was substantially greater when exposures were measured in reservoir dust. Using NAS, Can f 1 was detected in 13 of 16 (81%) homes with a dog and 54 of 99 (55%) homes without a dog; Fel d 1 was detected in 25 of 29 (86%) homes with a cat and 58 of 85 (68%) homes without a cat.

We found significant correlations between cat halo counts and reservoir Fel d 1 (living room floor: $r = 0.31$, $P = .001$, Fig 1, A; mattress: $r = 0.36$, $P = .001$) and between dog halo counts and Can f 1 concentrations in living room floor ($r = 0.20$; $P = .03$; Fig 1, B), but not in mattress dust ($r = 0.16$; $P = .10$). There was no significant relationship between mite halo counts and reservoir dust Der p 1 concentrations ($P > .50$; Fig 1, C).

Asthma severity

There was no relationship between asthma severity determined by FEV₁ and eNO and allergen sensitization and exposure (NAS or dust reservoir). The rest of the analysis explores the effects of sensitization and exposure on PD₂₀FEV₁.

Combined effects of sensitization with exposure. We found a significant effect of sensitization with high allergen exposure on PD₂₀FEV₁ for any allergen when exposure was measured in dust reservoirs ($F[3,60] = 2.98$; $P = .04$), but not when exposure was measured by NAS ($F[3,60] = 1.60$; $P = .20$). For individual allergens,

TABLE I. Demographic characteristics of study population

Demographic characteristics	
Age, mean (range)	52 (13-73)
Sex (male/female)	48 (41%)/69 (59%)
Nonsmokers/smokers (%)	105 (90%)/12 (10%)
Receiving inhaled steroids	90 (78%)
Dose of ICS, mean, median (range)	928 µg, 800 µg, (100-3000)
FEV ₁ % predicted	Normal 48%, mild 32%, moderate 15%, severe 5%; N = 116; Mean, 81; Median, 82; Range, 23-146
eNO (ppb)	N = 90; GM, 7.80; 95% CI, 6.77-9.00 Range, 1.43-65.5
PD ₂₀ FEV ₁	Normal 1%, mild 27%, moderate 48%, severe 24%; N = 71; GM, 0.42; 95% CI, 0.30-0.59 Range, 0.027-6.994
Allergen sensitization, N (%)	
Cat	45 (39%)
Dog	40 (34%)
House dust mite	59 (50%)
Allergen reservoir dust exposure (high levels), N (%)	
Cat	31 (27%)
Dog	22 (19%)
Mite	67 (57%)

similar effects on PD₂₀FEV₁ of sensitization with exposure were seen, whether exposure was defined by reservoir dust thresholds or by NAS counts in the uppermost tertile. For clarity, in calculations using dust reservoir exposures, the effects of cat allergen ($F[3,63] = 2.91$; $P = .04$) and mite allergen ($F[3,63] = 2.83$; $P = .04$) on PD₂₀FEV₁ were significant, whereas the effect of dog allergen was not ($F[3,64] = 0.57$; $P = .63$). The estimated marginal means from these analyses are shown in Table III. None of the planned contrasts were significant ($P \geq .1$).

Separate effects of sensitization, exposure, and their interaction. Sensitization, but not exposure to any allergen in the reservoir dust, conferred lower PD₂₀FEV₁ values (ie, more reactive airways). A similar picture emerged for cat and mite allergen. When exposure was defined as having a NAS count in the upper tertile, similar results were obtained for any allergen and for mite allergen.

When NAS exposure data were used for cat allergen, the effects of both cat sensitization ($F[1,61] = 4.681$; $P = .034$) and exposure ($F[1,61] = 3.087$; $P = .084$) were significant. This result was confirmed when sensitization was defined as the specific IgE titer and exposure as continuous variable (allergen concentration). However, there was no significant interaction between cat sensitization and exposure to cat. In this model, increasing exposure to cat allergen was associated with improving bronchial reactivity in patients who were not cat-sensitized.

TABLE II. Allergen exposures measured by reservoir allergen concentrations and NAS counts*

	Fel d 1				Can f 1				Der p 1			
	N	Living room floor	Mattress	NAS	N	Living room floor	Mattress	NAS	N	Living room floor	Mattress	NAS
All	109	2.8 (1.5, 5.3)	0.8 (0.5, 1.5)	2 (0, 49)	110	0.8 (0.5, 1.4)	0.33 (0.2, 0.5)	1 (0, 64)	107	1.1 (0.6, 1.9)	0.5 (0.3, 0.9)	1 (0, 69)
Pet owner	29	258‡ (152, 439)	45.5‡ (23.5, 88.0)	6§ (0, 49)	14	75.3‡ (19.4, 292)	14.2‡ (3.6, 55.3)	6§ (0, 19)	40	1.0 (0.4, 2.6)	0.6 (0.3, 1.2)	1 (0, 68)
Nonowner	79	0.6‡ (0.4, 0.8)	0.2‡ (0.1, 0.3)	1§ (0, 46)	95	0.46‡ (0.3, 0.7)	0.19‡ (0.2, 0.3)	1§ (0, 64)	66	1.1 (0.5, 2.2)	0.5 (0.3, 0.9)	1 (0, 7)
Ratio†		495 (233, 1048)‡	226 (109, 468)‡	6§		188 (61, 583)‡	73 (31, 174)‡	6§				

*Reservoir exposures are GM $\mu\text{g/g}$ (95% CI). NAS counts are median (range) values.

†Ratio is the ratio of exposure for pet owners versus non-pet owners for each of the allergens Fel d 1 and Can f 1. For reservoir dust, the ratio of GM exposures is given with 95% CI. For NAS exposures, the ratio of median exposures is given.

Significant differences in exposure between pet owners and nonowners for each pet allergen are shown: ‡ $P < .001$ (t test); § $P = .002$ (Mann-Whitney).

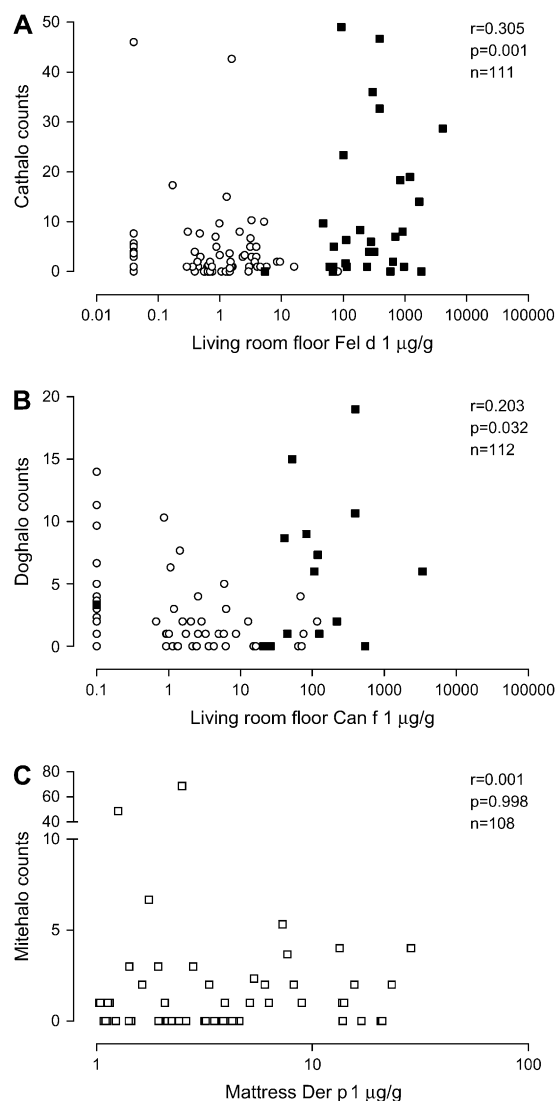


FIG 1. Reservoir dust allergen concentrations and NAS counts for each allergen. Correlations are Spearman rank. ■, Homes with pets; ○, homes without pets.

Inhaled particle autologous IgE and IgG₄ counts

Pet owners had higher numbers of IgE and IgG₄-stained halos than subjects without a pet (Table IV). There was no relationship between NAS-IgE or NAS-IgG₄ with exposures determined by reservoir dust concentrations.

There was a significant positive effect on NAS-IgE of the interaction between cat sensitization and NAS-cat exposure ($\beta = 0.124$; SE = 0.06; $P = .04$). This interaction is illustrated by categories of cat sensitization and exposure in Fig 2. Thus, as cat sensitization and exposure increase, so does NAS-IgE. The individual effects of cat sensitization and exposure were not significant ($P > .1$). There was a significant effect of dog sensitization ($\beta = -0.031$; SE = 0.015; $P = .04$) but not NAS-dog exposure. The thresholds for each tertile were as follows: $Y_{(\text{lower})} \geq -1.01$; $-2.56 \leq Y_{(\text{middle})} \leq -1.01$; $Y_{(\text{upper})} \leq -2.56$. The effects of sensitization and exposure to mite were not significant ($P > .2$).

There were significant positive effects on NAS-IgG₄ of NAS-cat exposure ($\beta = 0.29$; SE = 0.13; $P = .02$), NAS-dog exposure ($\beta = 0.53$; SE = 0.22; $P = .01$), and NAS-mite exposure ($\beta = 0.44$; SE = 0.23; $P = .05$). The thresholds for each quartile were as follows: $Y_{(\text{lowest})} \leq 0.54$; $0.54 \leq Y_{(\text{lower})} \leq 1.63$; $1.63 \leq Y_{(\text{upper})} \leq 2.87$; $Y_{(\text{highest})} \geq 2.87$. There were no effects of allergen sensitization on NAS-IgG₄.

NAS-IgE and NAS-IgG₄ counts bore no relationship to any measure of asthma severity ($P > .2$).

DISCUSSION

Reservoir dust allergen concentrations have been used to demonstrate that subjects with asthma exposed to allergens to which they are sensitized have more severe disease.^{10,11,16} Although our data show significant effects of sensitization with exposure in the reservoir dust on airway reactivity, this initially appears to be primarily because of allergen sensitization rather than exposure. However, in our previous study, the interaction between

TABLE III. Independent effects of sensitization and exposure (dust) to any allergen, cat, and mite allergen on bronchial reactivity*

PD ₂₀ FEV ₁	Estimated marginal means, GM (95% CI)				ANOVA		
	NS/NE	S/NE	NS/E	S/E	Sensitization	Exposure	Interaction
Any allergen†	0.36 (0.12, 1.11) N = 7	0.22 (0.11, 0.46) N = 19	0.83 (0.45, 1.55) N = 35	0.32 (0.18, 0.55) N = 43	F(1,60) = 4.29 P = .043	F(1,60) = 1.80 P = .185	F(1,60) = 0.13 P = .716
Fel d 1†	0.41 (0.24, 0.68) N = 46	0.24 (0.13, 0.42) N = 32	1.11 (0.47, 2.67) N = 22	0.41 (0.13, 1.27) N = 9	F(1,60) = 3.75 P = .058	F(1,60) = 2.57 P = .114	F(1,60) = 0.35 P = .559
Der p 1†	0.49 (0.25, 0.98) N = 21	0.24 (0.11, 0.52) N = 23	0.75 (0.40, 1.41) N = 34	0.24 (0.13, 0.45) N = 32	F(1,58) = 10.94 P = .002	F(1,58) = 0.11 P = .745	F(1,58) = 0.60 P = .443

*A categorical variable combining sensitization with exposure was used to assess the relationship with asthma severity. The estimated marginal mean PD₂₀FEV₁ for each category is shown on the *left*. Contrast analysis did not show significant differences between the groups. The separate effects of sensitization and exposure on bronchial reactivity after adjustment for confounders are shown on the *right*.
†Smoking is a significant confounder; P < .01.

TABLE IV. IgE-staining and IgG₄-staining halo counts in all individuals, in those with and without pets, and in pet owners who are sensitized or not sensitized to their pets*

	All	Pet owners	Non-pet owners	Sensitized pet owners	Nonsensitized pet owners
n	116	41	72	19	29
IgE	0 (0, 36)	1† (0, 36)	0† (0, 22)	2§ (0, 36)	0§ (0, 16)
IgG ₄	2 (0, 278)	3‡ (0, 278)	2‡ (0, 83)	10 (0, 278)	2 (0, 65)

*Values are median (minimum, maximum).
†P = .025; ‡P = .027; §P = .053; ||P = .058 (Mann-Whitney).

sensitization and exposure adversely affected airway reactivity, lung function, and eNO.¹⁰ This discrepancy is most likely a result of the larger number of study participants in the previous study; the current study is simply unable to demonstrate an effect of exposure (NAS) on severity.

Personal exposure to aeroallergens is complex and is affected by multiple factors (eg, particle aerodynamic size and allergen content, breathing rate, nasal caliber, dust disturbance, room temperature, and ventilation rate). Nasal air samplers offer theoretical advantages over reservoir dust and standard air samplers: they can detect inspired mite allergen-bearing particles under natural conditions in bed,²² and exposure is assessed directly from the position of the human nose. This enables the measurement of changes in exposure occurring within a person's breathing zone.²⁴

However, our data suggest that NAS is less useful than reservoir dust sampling for examining the relationship between allergen exposure and asthma severity. To explain this, 3 factors need to be considered: particle size, the number of sample replicates, and the time frame and conditions under which nasal air sampling was conducted.

Nasal air samplers detect 50% of particles >5 μm.²⁰ Smaller particles may bypass the nasal samplers, causing symptoms, yet failing detection. Furthermore, the detection of larger particles may be relatively hindered in patients with rhinitis with nasal air flow limitation.

By using 6 replicate NAS samples, we have previously demonstrated a correlation between mite allergen concen-

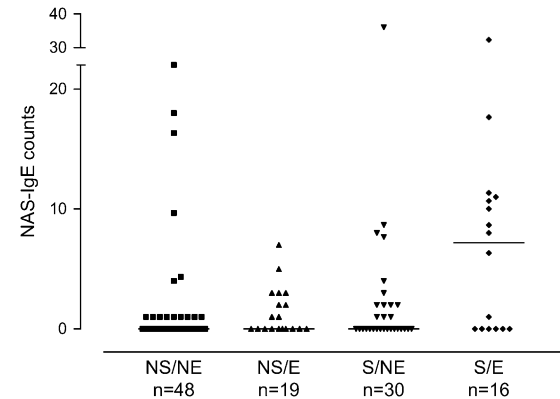


FIG 2. Relationship among NAS-IgE counts, sensitization, and exposure to cat. Lines represent the median value.

tration in reservoir dust and personal inhaled exposure.²² This finding was not confirmed in the current study. However, asking subjects to wear multiple replicate NAS for each allergen is impractical and impedes compliance. Therefore, in the current much larger study, we decided to use 1 sample per allergen, which may not reflect the cumulative exposure to the same degree as the reservoir concentration or repeated NAS counts.

Previous studies observed a 100-fold to 400-fold difference in cat or dog reservoir dust allergen concentrations between homes with and without pets.^{29,31-33} However, the magnitude of these differences as measured by NAS

appears smaller and is similar to that reported for standard air sampling.^{32,33} Although only a small proportion of reservoir dust is airborne at any one time, the apparent small difference in exposure between these 2 groups suggests that NAS as used in the current study may be underestimating the cumulative exposure to pet allergens.

An additional potential confounder may be that exposure to allergens occurs throughout the home, in work environments, and in schools, around the clock.³⁴ We assessed ambient personal exposure at a single time point and assumed that this would be a representative measure of average personal exposure, which may not be the case. For example, in epidemiological studies of the health effects of air pollution, changes in 24-hour exposures to particulate matter have demonstrable adverse health effects.^{35,36} Time frames may be different for allergens compared with particulate matter and may differ between allergens. NAS has proven to be a useful measure of personal allergen exposure in studies for which the time frame of exposure is easy to define.^{37,38} For studies of asthma severity, such a definition does not exist, and the time frames used are influenced by practical considerations.

Peak allergen exposures cause immediate symptoms of hypersensitivity in some individuals. Such peaks are relatively simple to determine in the occupational setting, when workers are exposed to an allergen unique to the workplace that can be easily measured.³⁹ However, domestic allergen exposure is more ubiquitous,⁴⁰ more physically inhomogeneous, and harder to characterize. Serial nasal air sampling could provide a better measure of average cumulative exposure and could also provide task-dependent measures of peak exposure. Such an approach could potentially explain better the relationship among disease severity, exposure, and sensitization. However, this would be expensive and impractical for large clinical studies.

The NAS-IgE sample can be conceptualized as a composite measure of both sensitization and exposure to any inhaled allergen. However, this measure bore no relationship to asthma severity. The high frequency of low counts even among individuals sensitized to common aeroallergens demonstrates that if a single measure is taken, the technique in its current form is of low sensitivity.

In areas where cats and dogs are the major source of sensitizing allergens, living with a cat may protect from asthma and sensitization to cat.^{41,42} This may be mediated through the development of modified T_H2-type tolerance; cat-exposed individuals have higher levels of Fel d 1-specific IgG and IgG₄.^{41,43} Dog ownership may similarly be protective,⁴¹ although it remains unclear which mechanism is implicated. We demonstrated relationships between personal inhaled cat and dog exposure and NAS-IgG₄. This suggests that individuals can manifest an IgG₄ response to dog allergens as well as to cat allergens. The development of dual antibody staining would help confirm this. Within this context, it is worth noting that exposure to cat allergen did have an effect on BR, with results suggesting that increasing exposure is associated

with improving airway reactivity in patients who were not cat-sensitized. This raises a possibility that at least amongst some patients with asthma who are not sensitized to cat, living with a cat may be associated with improved asthma control. If this is proven correct, then removal of cat in such patients may lead to deterioration in asthma control.

In conclusion, nasal air samplers are sensitive tools for exploring changes in personal allergen exposure when the allergen is easily raised and when the relevant time frame of exposure measurement can be defined.^{37,38,44,45} However, for the study of the relationship between allergen exposure and asthma severity, NASs are unable to provide a sufficient measure of cumulative exposure; here, reservoir dust allergen concentrations remain the method of choice.

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