

Airborne endotoxin in homes with domestic animals: Implications for cat-specific tolerance

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Background: Although endotoxin is known to increase symptoms in allergic individuals, early exposure might decrease sensitization. Similarly, the presence of an animal in the home has been associated with decreased sensitization to animal allergens. It has been suggested that the effect of animals could be explained by increased endotoxin exposure.

Objective: We sought to investigate the effects of domestic animals on airborne endotoxin.

Methods: By using a silent particle collector, air was sampled over 24 hours in homes with or without animals. The total volume sampled was approximately 1000 m³, which provides quantities of allergen and endotoxin that can easily be measured with standard assays.

Results: The quantity of endotoxin ranged from less than 0.5 to more than 500 pg/m³, whereas cat and dog allergen ranged from less than 0.002 to more than 5 ng/m³. Overall, the quantity of airborne endotoxin was not higher in homes with at least one animal. However, airborne endotoxin levels were significantly lower in homes with a cat compared with homes with a dog ($P < .001$). In keeping with this, there was a significant correlation between airborne Can f 1 and airborne endotoxin ($r = 0.50$, $P < .01$) but not between endotoxin and Fel d 1 ($r = 0.17$, $P = .27$).

Conclusions: The results demonstrate that endotoxin is present in the air of almost all homes. Although higher levels were seen in homes with a dog, similar levels might be present in homes with no animals. The results argue that the effects of cat ownership cannot be explained by increased exposure to endotoxin. (*J Allergy Clin Immunol* 2005;116:384-9.)

Key words: Airborne endotoxin, cats, dogs

Respiratory symptoms related to domestic animals are a significant health issue. However, in many studies the prevalence of IgE specific for cats or dogs is lower than for other major allergens, such as pollens or dust mites.¹⁻³ This is not due to inadequate exposure because the major allergens Fel d 1 and Can f 1 are found in schools, public

Abbreviations used

EU: Endotoxin units

ICD: Ion-charging device

places, and houses without a cat, as well as in those with an animal.⁴⁻⁷ Despite (or because of) this high allergen exposure, children raised in a house with an animal are less likely to become sensitized to animal allergens.⁸⁻¹²

One possible explanation for this paradoxical finding is that allergic families choose to avoid owning animals because of the perceived risk of sensitization.^{10,13} We have previously reported that high exposure to the cat allergen Fel d 1 induces a form of immune tolerance that is allergen specific.^{9,14,15} Alternatively, it has been argued that cats and other animals might increase agents such as bacterial LPS (endotoxin) in the home.¹² Endotoxin is known to favor a shift away from T_H2 responses in mice and might have the same effect on children.^{16,17} In keeping with this, children raised in close contact with farm animals (ie, with high endotoxin exposure) have less allergic disease.^{18,19} However, published reports are not consistent about the effects of pets on either floor or airborne endotoxin levels.^{15,20,21}

Measuring airborne allergen or endotoxin requires both sensitive assays and a technique for collecting airborne particles.^{22,23} The quantity measured is a function of the airborne concentration and the volume of air sampled. If the concentration in the air is low, low-volume samplers will require very sensitive assays and might still provide inadequate samples.^{22,24} On the other hand, a high-volume collector may sample the air repeatedly and thus underestimate the airborne concentration, whereas collectors with a fan are at risk of artificially increasing the flux of particles into the air.^{23,25} The ion-charging device (ICD) used here is silent but has a moderately high flow rate. The device has 3 stainless-steel collection plates from which the particles can be removed and analyzed. We have used this technique to measure airborne allergen levels in homes and airborne endotoxin levels in animal facilities.^{26,27} Those studies included validating the assay techniques and the collection efficiency of the device.

METHODS

Airborne sampling

The machines used for airborne sampling (Ionic Breeze Quadras from The Sharper Image, San Francisco, Calif) cycle between 2

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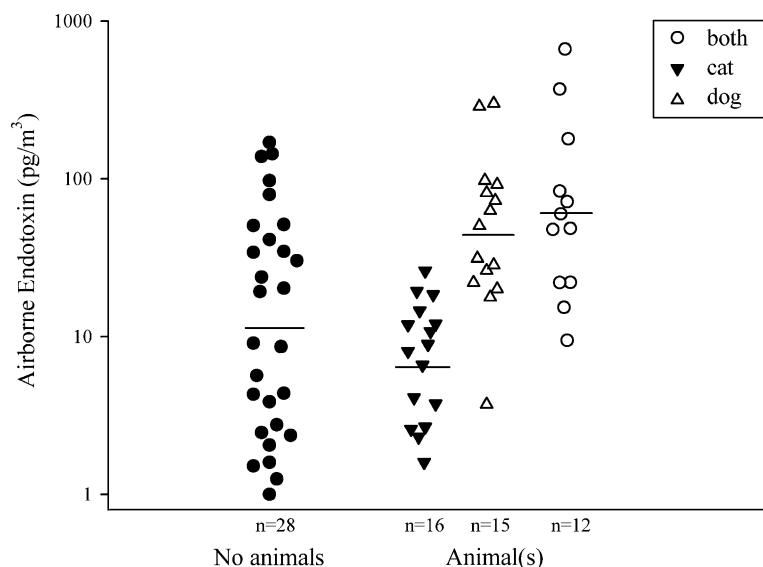


FIG 1. Airborne endotoxin concentrations in picograms per cubic meter calculated from quantities collected on the basis of 1 EU = 100 pg and a sampling rate of 0.67 m³/min (see the “Methods” section). Geometric means are indicated. Any subset of homes with dogs had significantly more airborne endotoxin than any subset without dogs.

distinct flow rates. For each device, we timed the periods P_1 and P_2 of each rate. By using a vanometer, the wind speed was measured at the center of 114 squares, each with an area of 9 cm², on a 2-dimensional grid placed orthogonal to and directly in front of the machine. These speeds were averaged and multiplied by the measurement area to determine the flow rate at each speed, V_1 and V_2 . The flow rate of each device was calculated as follows: $(P_1V_1 + P_2V_2)/(P_1 + P_2)$ in cubic meters per minute. The average flow rate of the 14 devices used in this study was 1.48 ± 0.09 m³/min.^{26,27}

A 20 L/min air-sampling pump and an ICD were run in parallel in a room with artificially disturbed dust (by using a vacuum cleaner without a filter) for 10-minute periods ($n = 8$) to determine the collection efficiency of the devices. The 20 L/min pump collected airborne particles by using the same prefilter as was used to clean the collection plates of the ICDs. All samples were extracted overnight in 2 mL of PBS and assayed for endotoxin and Fel d 1. The flow rates of the 2 devices and the amount of endotoxin and cat allergen measured were used to determine the collection efficiency for ICDs. The mean collection efficiency was $40.6\% \pm 9.0\%$ for endotoxin and $51.7\% \pm 12.0\%$ for Fel d 1, which were not significantly different. For the purposes of comparison with other studies, an estimated sampling rate of 0.67 m³/min was used, the product of the flow rate and a mean particle collection efficiency of 45%. Using this estimated sampling rate, we can convert values for the total quantities of airborne endotoxin or allergen collected to airborne concentrations (Figs 1-3).

All sampling used 2 ICDs in parallel running for 24 hours and placed at least 6 feet apart and at least 4 feet from the wall. In each case, the stainless-steel plates of the 2 ICDs were removed and cleaned with a series of 3 filters (Millipore prefilters, AP20, 35 mm; Millipore Corporation, Bedford, Mass) dampened with sterile water. Each filter was placed in a 3-mL syringe and extracted overnight at 4°C. The 3 filters from the first ICD were extracted in 2 mL of 1% BSA in PBS-Tween for measuring Can f 1 and Fel d 1, whereas those from the latter were extracted in 2 mL of endotoxin-free PBS for measuring endotoxin. In preliminary experiments 2 ICDs were run in parallel and both were assayed for either endotoxin or Fel d 1, and

there was a close correlation between samples for both endotoxin ($n = 56$, $r = 0.91$) and Fel d 1 ($n = 44$, $r = 0.93$).

Domestic sampling

A total of 71 homes in Central Virginia were studied between November 2003 and May 2004 to collect dust and carry out air sampling for 24 hours. Because seasonal variation has been reported for endotoxin, 43 homes were studied both in November-December and April-May. A floor dust sample was also collected with a Hoover handheld vacuum.

Animal room sampling

We sampled 20 mouse rooms from 4 different animal facilities (vivariums) at the University of Virginia. Each room was sampled at least twice. A variety of cage types are used, but for the purposes of this study, we have distinguished only between open cages, which have only a metal grill to prevent the animals from exiting the cage, and filter-topped cages of any configuration. The detailed methods have been published elsewhere.²⁷ All animals were used for research studies that had been approved by the University of Virginia Institutional Animal Care and Use Committee.

Assays

Samples were assayed for Fel d 1 and Can f 1 by using 2-site mAb-based ELISAs (Indoor Biotechnologies, Inc, Charlottesville, Va), which are sensitive to 1 ng/mL, and for endotoxin with the Limulus Amoebocyte Lysate test QCL 1000, which is sensitive to 0.3 endotoxin units (EU)/mL (equivalent to 30 pg of endotoxin/mL; Bio-Whittaker/Cambrex). Because extract freeze-thaw cycles are associated with a significant decrease in endotoxin concentration, samples were assayed for endotoxin immediately on extraction. The buffer used for extraction was used in each assay as a negative control and was less than the level of detection in all cases.

Statistical analysis

Because the exposure data had a log-normal distribution, all values were reported as geometric means with 95% CIs, and statistics

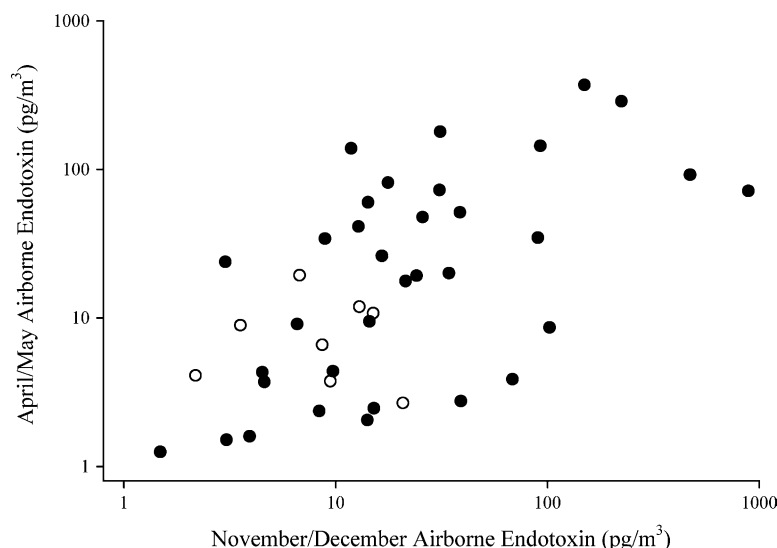


FIG 2. Airborne endotoxin was measured in 43 homes on 2 separate occasions 4 months apart. Although there was considerable variation between the 2 samples, the correlation was: $r = 0.57$, $P < .001$. For homes with cats, shown with open circles, each sample was less than 30 pg/m^3 .

were performed on log-transformed data. Means were compared by using independent-sample t tests, whereas a least squares linear regression was used to assess the seasonal variation in airborne endotoxin, the correlation between airborne allergens and endotoxin, and the correlation between duplicate measurements for endotoxin and cat allergen. A P value of less than .05 was considered significant. All statistical analyses were performed with SPSS 11 (SPSS Inc, Chicago, Ill).

RESULTS

Easily measurable concentrations of endotoxin and animal allergens were present in the floor dust samples. There was a wide range of values, from 0.82 EU/mg to 660 EU/mg, and overall, there was no significant effect of animal ownership (Table I). There were large differences in the concentration of cat and dog allergens, which was in keeping with the presence of animals.

The results for airborne endotoxin also showed no overall difference between homes with animals and homes without animals (Table II). The same data are presented as airborne concentrations (Fig 1). When the results were analyzed by the species of animal present, there were highly significant differences. Homes with a cat or cats had significantly lower airborne endotoxin levels than homes with a dog or with both species (Fig 1). In 43 houses airborne sampling for endotoxin was carried out twice, first in November-December and again in April-May (Fig 2). Overall, there was a good correlation between the 2 measurements ($r = 0.57$, $P < .001$). In particular, the values in homes with a cat were consistently lower (ie, $<30 \text{ pg/m}^3$). Comparing airborne dog allergen levels with airborne endotoxin levels showed a significant positive correlation ($r = 0.56$, $P < .001$; Fig 3, A). The association was not significant between endotoxin and cat allergen ($r = 0.13$, $P = .33$; Fig 3, B).

Presenting the results as endotoxin collected over 24 hours allows comparison between different homes and with animal facilities sampled in the same way. The results show that endotoxin exposure in homes is lower than in animal rooms where rats or mice are kept without a filter top on the cage. However, in animal rooms where cage tops are present, which is the case for the majority of animal facilities, the mean endotoxin airborne concentration was lower than that for homes (Table III).

DISCUSSION

In many studies the prevalence of IgE antibodies specific for cat or dog allergen is lower than for other major allergens, such as pollens or dust mites.¹⁻³ This is not due to inadequate exposure because (1) the phenomenon is more marked among children living in a house with a cat,⁸⁻¹² (2) the allergens are present and airborne continuously, and (3) the major allergens Fel d 1 and Can f 1 are found in schools, public places, and houses without animals, as well as those with an animal. Our data show that the presence of a cat in the home does not increase airborne endotoxin levels. Thus the allergen-specific tolerance to cat allergens cannot be attributed to increased endotoxin exposure in homes with a cat.

Inevitably, any sampling technique that collects a quantity of allergen or endotoxin that can be confidently measured will alter the particles present in the air. In addition, it is well established that the airflow created by a high-volume air filter can increase airborne allergen levels.²³ Thus all methods of measuring airborne concentrations of allergen or endotoxin involve a compromise. The particle collector used here has several disadvantages and some major advantages. The disadvantages are (1) those associated with high-volume sampling and (2) that

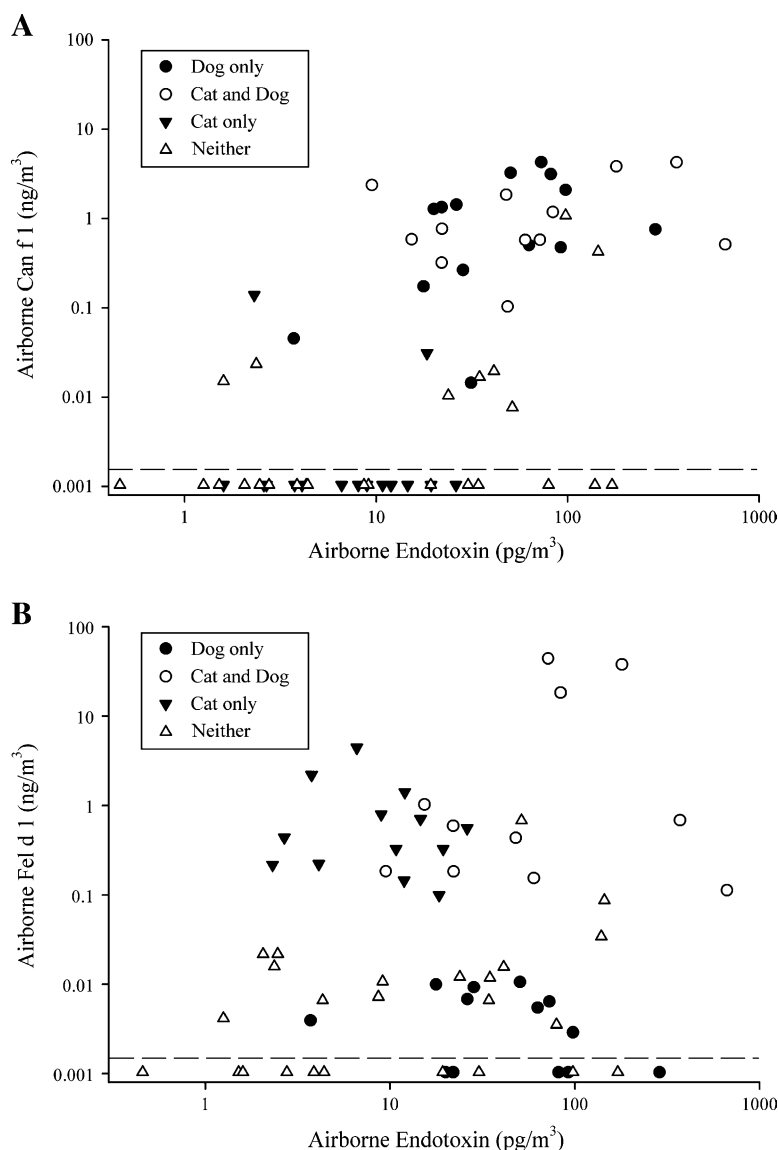


FIG 3. A, Airborne dog allergen concentration in nanograms per cubic meter compared with airborne endotoxin concentration in picograms per cubic meter ($r=0.56$, $P<.001$). **B,** Airborne cat allergen concentration in nanograms per cubic meter compared with airborne endotoxin concentration in nanograms per cubic meter ($r=0.17$, $P=.27$).

the interpretation of the quantity collected requires an estimate of the efficiency with which particles are collected. The advantages of the device are that (1) it is silent and therefore well accepted for use in any room, including bedrooms; (2) sampling of particles off the stainless-steel plates is simple and very consistent (this is not possible with most devices designed to clean the air, including all high-efficiency particulate air filters); and (3) it collects particles from large volumes of air, but because of the wide aperture, the velocity of air coming out is relatively low.

In preliminary experiments sampling air at 18 L/min for 2 to 6 hours, we were not able to detect significant endotoxin levels in most houses. Other groups have

successfully measured airborne endotoxin levels by using very low-volume sampling (ie, 2 L/min).^{22,28} However, that required extrasensitive assays and extensive precautions to avoid endotoxin contamination. The collector used here has no electrical safety concerns. Most pumps used for collecting airborne allergen are not approved as domestic appliances and therefore should not be left in a home without the presence of an investigator. The range of results observed (ie, from <5 to >5000 EU/24 hours or <0.5 to >500 pg/m³) is such that small differences in the estimated collection efficiency (ie, between 41% and 52%) would not affect the interpretation of our results.

In an additional experiment (data not shown), airborne endotoxin and Fel d 1 levels were measured before and

TABLE I. Floor dust concentration of endotoxin and allergens*

	N	Endotoxin (EU/mg)†	Fel d 1 (μg/g)	Can f 1 (μg/g)
No animals	23	49.8 (29.9-82.9)	2.5 (1.3-4.7)	2.3 (1.4-4.0)
Animals	39	63.9 (47.1-86.8)	25.1 (7.9-79.9)	49.4 (17.2-142)
Cat(s) only	13	82.8 (45.3-151)	583 (201-1690)	0.65 (0.24-1.7)
Dog(s) only	15	49.9 (31.3-79.5)	0.52 (0.24-1.1)	405 (226-728)
Both species	11	66.1 (39.5-110.7)	121 (36.1-405)	315 (169-586)

*All values are presented as geometric means (95% CIs).

†Endotoxin levels were not significantly different between cats and dogs ($P = .189$) or cats and no animals ($P = .221$).**TABLE II.** Airborne quantity of endotoxin and allergens collected in 24 hours*

	n	Endotoxin (EU/24 h)†	Fel d 1 (ng/24 h)	Can f 1 (ng/24 h)
No animals	28	115 (61-217)	6.6 (4.9-8.8)	3.3 (2.7-4)
Animals	43	240 (155-372)	102 (64-162)	138 (87-219)
Cat(s) only	16	68 (44-105)	488 (361-660)	3.4 (2.3-4.9)
Dog(s) only	15	447 (250-800)	4.7 (3.6-6.1)	777 (566-1067)
Both species	12	588 (282-1230)	1076 (545-2126)	1030 (790-1342)

*All values are presented as geometric means (95% CIs).

†Homes with dogs had higher airborne endotoxin than homes with cats ($P < .001$) or homes with no animals ($P = .003$), as did homes with both animals (vs homes with cats, $P < .001$; vs homes with no animals, $P = .005$).**TABLE III.** Airborne endotoxin in homes and animal rooms

	n	EU/24 h (GM)
Homes without animals	28	115 (61-217)
Homes with animals	43	240 (155-372)
Mouse rooms (open cages)	8	1930 (752-4940)*
Mouse rooms (filter tops on cages)	20	47.8 (31.9-71.6)†

GM, Geometric mean.

*Significantly higher than homes with or without animals ($P < .001$).†Significantly lower than homes with animals ($P < .001$) or without animals ($P = .024$).

after disturbance of dust in an experimental room by using a domestic vacuum cleaner without a filter. The results suggested that 90% of both airborne endotoxin and cat allergen levels fell within 10 minutes. The rapid falling rates of both endotoxin and cat allergen suggest that the level of disturbance is as important as the concentration in reservoirs of dust. The observation that endotoxin levels in the floor dust of houses with cats or dogs are similar, yet the airborne levels are significantly different, might suggest that dogs were a greater cause of disturbance.

Differences in the quantity of endotoxin either airborne or in the floor dust of houses with a cat cannot explain why the presence of a cat in the house is associated with a form of immune tolerance. However, this is not to say that airborne endotoxin is irrelevant to the response. In mice the immune response to inhaled ovalbumin can be suppressed or changed by high exposure to endotoxin, but the IgE antibody response is enhanced by small quantities of endotoxin.¹⁶ We have found airborne endotoxin in almost all homes, and this might be sufficient to act as an adjuvant for responses to inhaled allergens.²⁹ At

present, it remains unclear whether inhaled endotoxin in homes contributes either to sensitization or symptoms. The concentrations reported here in homes are higher than the concentrations reported to give rise to symptoms among animal handlers.²⁸ However, those studies used low-volume sampling and reported a much smaller range of results than we have found here or in animal facilities.²⁷ Furthermore, recent short-term challenge studies found that doses of less than 10,000 EU produced very little immediate change in the lungs.³⁰

Some authors have implied that both the effects of cow ownership in Europe and the paradoxical effects of cat ownership are in keeping with the hygiene hypothesis. Our data argue in favor of a completely different interpretation of the effects of cat ownership. In our studies on 4 different cohorts, the effect of cat ownership has been cat specific. In particular, cat ownership has no effect on the IgE antibody response to dust mite allergens.^{9,15} In addition, the immune response to Fel d 1 includes the IL-4-dependent isotype IgG4.^{9,10} Thus the nonallergic response to cat has the features of a modified T_H2 response and not the T_H1 response that would be predicted if the tolerant response was related to increased endotoxin exposure.¹⁶⁻¹⁸

It is important to recognize that there are major differences in the ways that cats and dogs are kept, and our results might be relevant to specific housing conditions. In New Zealand the floor dust levels of endotoxin in homes with or without cats (13.7 vs 17.4 EU/mg, not significant) were lower than the levels seen here.¹⁵ Thus we could be looking at 2 different phenomena overlapping in different studies. The first effect is tolerance induced specifically by cat allergen exposure, whereas the second, a nonspecific effect of animal ownership, including dog ownership,

could reflect increased exposure to endotoxin or other bacterial products.

REFERENCES

- Roost HP, Kunzli N, Schindler C, Jarvis D, Chinn S, Perruchoud AP. Role of current and childhood exposure to cat and atopic sensitization. European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999;104:941-7.
- Sears MR, Herbison GP, Holdaway MD, Hewitt CJ, Flannery EM, Silva PA. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. *Clin Exp Allergy* 1989;19:419-24.
- Lewis SA, Weiss ST, Platts-Mills TA, Syring M, Gold DR. Association of specific allergen sensitization with socioeconomic factors and allergic disease in a population of Boston women. *J Allergy Clin Immunol* 2001;107:615-22.
- Sporik R, Ingram JM, Price W, Sussman JH, Honsinger RW, Platts-Mills TA. Association of asthma with serum IgE and skin test reactivity to allergens among children living at high altitude. Tickling the dragons breath. *Am J Respir Crit Care Med* 1995;151:1388-92.
- Almquist C, Larsson PH, Egmar AC, Hedren M, Malmberg P, Wickman M. School as a risk environment for children allergic to cats and a site for transfer of cat allergen to homes. *J Allergy Clin Immunol* 1999;103:1012-7.
- Custovic A, Green R, Taggart SC, Smith A, Pickering CA, Chapman MD, et al. Domestic allergens in public places. II: Dog (Can f1) and cockroach (Bla g 2) allergens in dust and mite, cat, dog and cockroach allergens in the air in public buildings. *Clin Exp Allergy* 1996;26:1246-52.
- Perzanowski MS, Ronmark E, Nold B, Lundback B, Platts-Mills TA. Relevance of allergens from cats and dogs to asthma in the northernmost province of Sweden: schools as a major site of exposure. *J Allergy Clin Immunol* 1999;103:1018-24.
- Hesselmar B, Aberg N, Aberg B, Eriksson B, Bjorksten B. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy* 1999;29:611-7.
- Platts-Mills T, Vaughan J, Squillace S, Woodfolk J, Sporik R. Sensitization, asthma, and a modified Th2 response in children exposed to cat allergen: a population-based cross-sectional study. *Lancet* 2001;357:752-6.
- Perzanowski MS, Ronmark E, Platts-Mills TA, Lundback B. Effect of cat and dog ownership on sensitization and development of asthma among preteenage children. *Am J Respir Crit Care Med* 2002;166:696-702.
- Custovic A, Hallam CL, Simpson BM, Craven M, Simpson A, Woodcock A. Decreased prevalence of sensitization to cats with high exposure to cat allergen. *J Allergy Clin Immunol* 2001;108:537-9.
- Ownby DR, Johnson CC, Peterson EL. Exposure to dogs and cats in the first year of life and risk of allergic sensitization at 6 to 7 years of age. *JAMA* 2002;288:963-72.
- Anyo G, Brunekreef B, de Meer G, Aarts F, Janssen NA, van Vliet P. Early, current and past pet ownership: associations with sensitization, bronchial responsiveness and allergic symptoms in school children. *Clin Exp Allergy* 2002;32:361-6.
- Reefer AJ, Carneiro RM, Custis NJ, Platts-Mills TA, Sung SS, Hammer J, et al. A role for IL-10-mediated HLA-DR7-restricted T cell-dependent events in development of the modified Th2 response to cat allergen. *J Immunol* 2004;172:2763-72.
- Erwin EA, Wickens K, Custis NJ, Siebers R, Woodfolk JA, Barry D, et al. Cat and dust mite sensitivity and tolerance in relation to wheezing among children with high exposure to allergens. *J Allergy Clin Immunol* 2005;115:74-9.
- Eisenbarth SC, Piggott DA, Huleatt JW, Visintin I, Herrick CA, Bottomly K. Lipopolysaccharide-enhanced, toll-like receptor 4-dependent T helper cell type 2 responses to inhaled antigen. *J Exp Med* 2002;196:1645-51.
- Gereda JE, Leung DY, Thatayatikom A, Strieb JE, Price MR, Klinnert MD, et al. Relation between house-dust endotoxin exposure, type 1 T-cell development, and allergen sensitization in infants at high risk of asthma. *Lancet* 2000;355:1680-3.
- Braun-Fahrlander C, Riedler J, Herz U, Eder W, Waser M, Grize L, et al. Environmental exposure to endotoxin and its relation to asthma in school-age children. *N Engl J Med* 2002;347:869-77.
- Gehring U, Bischof W, Fahlbusch B, Wichmann H-E, Heinrich J. House dust endotoxin and allergic sensitization in children. *Am J Respir Crit Care Med* 2002;166:939-44.
- Heinrich J, Gehring U, Douwes J, Koch A, Fahlbusch B, Bischof W, et al. Pets and vermin are associated with high endotoxin levels in house dust. *Clin Exp Allergy* 2001;31:1839-45.
- El Sharif N, Douwes J, Hoet PHM, Doeke G, Nemery B. Concentrations of domestic mite and pet allergens and endotoxin in Palestine. *Allergy* 2004;59:623-31.
- Park JH, Spiegelman DL, Gold DR, Burge HA, Milton DK. Predictors of airborne endotoxin in the home. *Environ Health Perspect* 2001;109:859-64.
- Luczynska CM, Li Y, Chapman MD, Platts-Mills TA. Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*). Measurements using cascade impactor, liquid impinger, and a two-site monoclonal antibody assay for Fel d 1. *Am Rev Respir Dis* 1990;141:361-7.
- Schweitzer IB, Smith E, Harrison DJ, Myers DD, Eggleston PA, Stockwell JD, et al. Reducing exposure to laboratory animal allergens. *Comp Med* 2003;33:486-92.
- Swanson MC, Agarwal MK, Reed CE. An immunological approach to indoor aeroallergen quantitation with a new volumetric air sampler: studies with mite, roach, cat, mouse, and guinea pig antigens. *J Allergy Clin Immunol* 1985;76:724-9.
- Custis NJ, Woodfolk JA, Vaughan JW, Platts-Mills TAE. Quantitative measurement of airborne allergens from dust mites, dogs, and cats using an ion charging device. *Clin Exp Allergy* 2003;33:986-91.
- Platts-Mills J, Custis N, Kenney A, Tsay A, Chapman M, Feldman S, et al. The effects of cage design on airborne allergens and endotoxin in animal rooms: high-volume measurements with an ion-charging device. *Contemp Top Lab Anim Sci* 2005;44:12-6.
- Pacheco KA, McCammon C, Liu AH, Thorne PS, O'Neill M, Martyny J, et al. Airborne endotoxin predicts symptoms in non-mouse-sensitized technicians and research scientists exposed to laboratory mice. *Am J Respir Crit Care Med* 2003;167:983-90.
- Liu AH. Endotoxin exposure in allergy and asthma: reconciling a paradox. *J Allergy Clin Immunol* 2002;109:379-92.
- Alexis NE, Lay JC, Almond M, Peden DB. Inhalation of low-dose endotoxin favors local T(H)2 response and primes airway phagocytes in vivo. *J Allergy Clin Immunol* 2004;114:1325-31.