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Prenatal exposure to household pets influences fetal IgE production

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Abstract

Background—Early life pet exposure may protect against allergic sensitization during childhood. Few studies have evaluated the effect of prenatal pet exposure on potential neonatal markers of allergic risk.

Objective—To investigate whether maternal exposure to pets affects cord blood IgE levels in a population-based, general risk, ethnically mixed birth cohort.

Methods—Pet keeping during pregnancy was ascertained from women residing in a defined area of Wayne County Michigan and recruited from five staff model obstetric clinics. Maternal venous blood was analyzed for total and allergen-specific IgE along with cord blood total IgE from 1049 infants.

Results—Compared to infants from households with no cats or dogs kept indoors during pregnancy, infants whose homes had either cats or dogs had significantly reduced mean cord IgE levels [0.34 IU/ml (95%CI 0.30–0.38) vs. 0.24 IU/ml (0.20–0.27) p = 0.025]. Similar effects were apparent in cat-only households [0.21 IU/ml (0.16–0.27), p = 0.020] and dog-only households [0.24 IU/ml (0.19–0.29), p = 0.045]. There was no effect on results when excluding mothers who reported avoiding pets due to allergy-related concerns.

Conclusion—Mothers with either cats or dogs in their home during pregnancy deliver children with lower cord blood IgE levels compared to mothers who do not live with these pets, supporting the hypothesis that pet exposure influences immune development in a manner that is protective for atopy and is operant even before birth.

Keywords

IgE; cord blood; atopy; dog; cat; pets; pregnancy; fetal; allergy; immune response

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Introduction

Studies suggest that exposure to domestic pets, especially cats and dogs, during early life decreases the risk of subsequent allergic sensitization or atopic disease. However, this protective effect is an area of controversy with additional conflicting reports showing elevated risk or lack of a relationship between pet exposure and atopy. Two published reviews summarize these contrasting studies and attribute the discrepant results primarily to nuances in study design, diverse study population characteristics and differences in strategies utilized to define pet exposure[1,2]. Furthermore, the mechanisms by which pet exposure may alter risk remain largely unknown.

It is becoming increasingly clear that the maternal environment during pregnancy has potential effects on the immune function of offspring. Although normal fetal immune function appears to be characterized by an IgE-promoting, Th2-skewed immune response[3], a gradual "maturation" toward balanced Th1-Th2 function is considered a critical determinant in limiting the development of atopy during childhood and later life[4]. The factors that determine the timing and degree of this maturational process are uncertain. However, immunocompetent cells in the fetus appear to be primed by exposure to allergens in their mother's environment as early as 22 weeks of gestation[5]. Also, maternal exposure to farm animals and environments rich in microbial compounds during pregnancy is associated with upregulated genetic expression of receptors related to the innate immune system in their children[6]. Finally, both B and T cell influenza antigen-specific responses in cord blood are apparent among children whose mothers receive flu vaccine during pregnancy[7]. These studies are consistent with the emerging concept that gestation is a time of active immune education and that fetal immune development is influenced by the maternal environment.

Elevated levels of cord blood IgE have been linked to an increased risk for subsequent allergen-specific IgE production or allergic disorders[8–10]. IgE cannot cross the placenta[11] and fetal IgE production begins as early as 11 weeks of gestation[12]. Therefore, the presence of high levels of IgE in cord blood indicate increased B cell isotype switching in the fetus.

One previously published study, utilizing a general risk birth cohort, suggested a protective effect of prenatal pet keeping on elevated IgE levels in children measured shortly after birth[13]

Our aim was to investigate whether maternal exposure to indoor pets, defined as keeping an indoor dog or cat, affects fetal IgE production using a general risk, ethnically mixed population.

Methods

Study Population

The Wayne County Health, Environment, Allergy and Asthma Longitudinal Study (WHEALS) is an ongoing unselected birth cohort study in southeastern Michigan designed to examine the relationships between early life exposures such as pets, infections and endotoxin and allergic diseases in early childhood. We recruited women between 21 and 49 years of age from a predefined geographic area who are in their second trimester of pregnancy, are seeing a Henry Ford Health System medical group clinician at one of five clinics, and plan to stay in the Detroit area for at least two years after delivery. Prior to meeting the women at the clinics to discuss participation, a letter introducing the study is mailed to them. Recruitment began in September 2003 and was completed in November 2007. There are 1258 women in the WHEALS study. Women are required to speak English

well enough to provide written informed consent. This research was approved by the Henry Ford Hospital IRB.

Assessment of Maternal Allergy and Asthma History

We interviewed women at the time of recruitment to obtain their pregnancy, asthma and allergy histories, as well as information about the asthma and allergy histories of their babies' fathers. Specific questions relevant to this report include: (1) "Since the time you learned you were pregnant have you owned or cared for any pets for more than 1 week in your home?" (2) "In your current household, have you ever intentionally not kept pets because someone who lives there is highly allergic to animals?" (3)"When you are near animals such as cats or dogs, do you ever start to cough, wheeze, get a feeling of tightness in your chest, start to feel short of breath, get a runny or stuffy nose or start to sneeze?" (4) "Do you have nasal allergies including hay fever and allergic rhinitis?" Those who said "yes" to (4) were then asked, (5) "Did a doctor ever diagnose you with hay fever, nasal allergies or allergic rhinitis?" All women were also asked: (6) "Have you ever had asthma?" For those who said "yes" to (6), we then asked, (7) "Did a doctor ever diagnose you with asthma?" Additional questions regarding self-reported race using the United States census categorization, education level, and household smoking were also included.

Assessment of Total and Allergen-specific IgE

Cord blood samples were collected in the delivery room. The serum was separated by centrifugation and frozen prior to analyses of total IgE. Measurements were performed using the Pharmacia UniCAP system (Pharmacia-Upjohn Diagnostic Division, Kalamazoo, MI) using the manufacturer's protocol for high sensitivity. The high sensitivity protocol provides an assay range of 0.01 to 100 IU/mL of IgE. One percent of all samples are reanalyzed in a different assay run on a different day to provide a precise estimate of inter-assay reliability over time. Thirty-four (3.2%) of our samples had undetectable measures of IgE and were assigned a value of 0.01 IU/ml.

Venous blood collected from participating mothers was analyzed for allergen specific and total IgE. We assessed these measures using maternal blood samples drawn in either the 2nd trimester of pregnancy (n=793) or at 1 month postpartum (n=198). Specific IgE levels to the following seven allergens were analyzed (Pharmacia CAP, Pharmacia Diagnostics AB): *Dermatophagoides farinae* (Derf), cat, dog, *Phleum pratense* (timothy grass), *Blatella germanica* (German cockroach), *Alternaria alternata*, and *Ambrosia artemisiifolia* (ragweed). Seroatopy was defined as a positive specific IgE (≥0.35 kU/L) to at least one of the above allergens.

Statistical Analysis

Group comparisons (those with cord blood measures vs. those missing cord blood IgE measurement) on categorical variables such as race and education level were done using chi-squared tests. A Student's t-test was used to compare mean age between the two groups. As IgE data was not normally distributed, maternal total IgE was analyzed using the nonparametric Wilcoxon rank sum test. Geometric means and 95% confidence intervals (95% CI) are presented to summarize the IgE data. Because the distribution of IgE data was skewed, linear regression modeling was performed using log transformed values of IgE. We had two main aims for this study: 1) to see if *any* indoor pet exposure had an effect on cord IgE levels and, 2) to investigate both the effect of number of pets and the type of pet exposure on cord IgE levels as thoroughly as our sample size would allow. For the first aim, we created a dichotomous exposure variable of any indoor pet(s) vs no pets. For the second aim, we used a series of exposure classification methodologies.

The first classification methodology included the Jonckheere-Terpstra test for trend to examine the effect of increasing numbers of cats only, dogs only and pets (number of dogs plus cats) on cord IgE levels. After this initial test, we then categorized pet exposure using another classification methodology by making one variable for dog exposure and, separately, one variable for cat exposure using the following three ordinal groups: (1) no dog or cats in the home; (2) 1 dog or 1 cat in the home; and (3) 2 or more dog(s)/cat(s) in the home. The third group was used since there were few multiple dog(s) and cat(s) households. After we found no significant difference between the 1 pet level and the 2 or more pet level, we then combined these groups for continued analysis. Interactions between the dog exposure and cat exposure variables was significant for both the 3-pet level ($p=0.002$) and 2-pet level ($p=0.005$) exposure categorizations.

Our final pet exposure classification methodology to address our second aim was based on an exclusive categorization scheme as follows: (1) no dog or cat exposure; (2) dog(s) exposure, but no cat exposure; (3) cat(s) exposure but no dog exposure; (4) both dog(s) and cat(s) exposure.

For all analyses, the referent category for pet exposure was “no indoor pets”.

We considered the following list of variables as possible effect modifiers: race, maternal smoking during pregnancy, baby’s sex, maternal dog seroatopy, maternal cat seroatopy, maternal atopy to any of the seven allergens tested (including dog and cat), birth weight and gestational age. Stratified analyses and interaction terms in linear regression models were used to assess possible effect modifiers. We then assessed potential confounders. A variable was considered to confound the association between pets and cord blood IgE if it was significantly related to cord IgE and, separately, to indoor pet status, as well as changed the effect of the association between pets and cord blood IgE by 10% or more when included in the linear regression model. Potential confounders evaluated were: race, maternal smoking during pregnancy, birth weight, gestational age, maternal history of asthma or allergy, paternal history of asthma or allergy and maternal history of allergic-like symptoms when around animals.

All analyses were performed using SAS for Windows version 9.1; SAS Institute, Cary, NC.

Results

A total of 1258 mothers that completed interviews during pregnancy were eligible for inclusion. Cord IgE data is currently available from 1049 (83%) infants. The remaining 209 (17%) subjects are excluded from analysis due to missed opportunities to obtain cord blood samples. The demographic and allergic history characteristics for those mothers included in the analysis and stratified for the presence or absence of indoor dog(s) or cat(s) are presented in Table I. Those included and excluded were similar in characteristics included in Table I except for slightly lower age (29.3 versus 30.3 years), higher college attendance (77.7% versus 67.5%), lower incidence of preterm birth at less than 37 weeks gestation (7.6% versus 14.5%) or birth weight less than 2500 grams (6.1% versus 13.6%) among mothers whose infant’s cord IgE was able to be collected. Interestingly, a higher proportion of indoor cat keeping (17.1% versus 11.0%) was also present among those mothers whose cord blood was obtained.

We defined being exposed as the presence of the pet inside the home at least 1 hour each day, meaning pet owners who keep dogs/cats almost exclusively outdoors are included in the category of “no indoor pets.” During pregnancy, 674 households had no indoor pets and 375 had dogs or cats in the home. Of these 375 households, 196 had dogs only, 118 had cats only, and 61 homes kept both dogs and cats in the home during pregnancy (Table II).

Compared to infants from households with no indoor cats or dogs during pregnancy, infants whose homes had a cat or dog had a significantly reduced mean cord IgE level [0.34 IU/ml (95%CI 0.30–0.38) vs. 0.24 IU/ml 0.20–0.27) $p < 0.001$]. (Table II). A similar effect was also observed among those infants in the subcategories of indoor dogs only and indoor cats only compared to the "no indoor pets" infants [0.24 IU/ml (0.19 – 0.29) and 0.21 IU/ml (0.16 – 0.27), $p = 0.003$ and 0.001 respectively]. Differences between these groups remained statistically significant after controlling for the confounder of African-American race. Interestingly, mean cord IgE levels in infants from 61 households possessing both indoor dogs and cats was between those of households containing no pets and those containing either only dogs or only cats. The mean cord blood IgE from these infants [0.30 IU/ml (0.20 –0.44)] was not significantly different than the group with no indoor pets [0.34 IU/ml (0.30 –0.38)], the cat-only [0.21 (0.16, 0.27)] or dog-only observations [0.24 (0.19, 0.29].

We also tested for a "dose-response" relationship in homes with multiple animals. Although, the data in Table III reflects a trend for lower cord IgE levels where households had more than one dog or cat compared to a single cat or dog, the differences were not statistically significant. Further, analyzing the number of pets/dogs/cats within homes with at least 1 animal failed to detect an increasing or decreasing trend in cord IgE levels. (Jonckheere-Terpstra trend test $p=0.98$ (cats), $p=0.25$ (dogs) and pets ($p=0.95$).

Cord IgE levels were higher among infants whose mothers reported a history of asthma or allergy and among infants whose mothers reported a history of clinical reactions when exposed to dog or cats. However, these factors did not influence the relationship of pet-keeping on cord IgE levels (Data not shown). We were concerned that selective avoidance of pets by families that have a history of allergy or asthma might influence our analysis. One hundred fifty-eight mothers (15.1%) indicated that pets were intentionally avoided due to allergy in a household member. When we repeated our analyses (Tables II and III) excluding these participants, the results were largely unaffected. (data not shown). Interestingly, 41 of 158 mothers (26%) indicating that they avoided ever having pets actually had a cat or dog in their home during pregnancy.

Discussion

Our results show that maternal exposure to indoor dogs or cats during pregnancy is associated with lower cord blood IgE levels in their offspring.

Our findings are largely in agreement with those of Kerkhoff et al[13]. In their study, heel prick IgE levels during the first week of life from 1027 infants living in the Netherlands were analyzed for associations to a variety of prenatal exposures including pets. When dogs or cats were present in the home during pregnancy, there was a lower likelihood of having a detectable level of total IgE at birth, although this was of borderline significance [OR (95% CI) 0.6 (0.4–1.0), $p =0.06$]. The association was more pronounced for dog [OR 0.5 (0.2–1.0), $p=0.06$] and a protective effect of cat keeping alone was not seen [OR 0.8 (0.5–1.3), $p=0.35$]. Their analysis was limited since only 9.3% of the children had detectable IgE levels with a limit of detection >0.5 IU/ml. In contrast, we found both dog and cat keeping were independently associated with lower cord IgE while analyzing IgE as a continuous variable with detectable levels (≥0.01 IU/ml) in greater than 95% of samples.

The clinical implication of an elevated cord blood IgE is that it may be a predictor of childhood allergen sensitization[10]. Therefore it is reasonable to speculate that early pet exposure may also effect the development of allergen-specific IgE sensitization later in life.

In the Tucson Children's Respiratory Study birth cohort, dog or cat keeping during infancy did not significantly influence the likelihood of a positive skin prick test to common

allergens at ages 6 and 11 years, nor total IgE levels at 9 months, 6 years and 11 years[14]. Interestingly, this study revealed a protective effect of dog ownership in infancy on the development of childhood asthma.

However, protective effects of pet keeping on allergic sensitization have been reported in several studies. A group from the Netherlands found that pet ownership during the first two years of life was associated with less pollen sensitization at 7 to 12 years[15]. In addition, cat ownership before 18 years of age was associated with lower rates of adult sensitization to outdoor allergens in an Australian population.[16] Protective effects of dog ownership at a median age of 2 months was associated with a decreased risk of sensitization to pollen allergens at age 4, while cat ownership was associated with a nonsignificant trend for protection in a Swedish birth cohort[17]. Finally, adult subjects in the European Community Respiratory Health Survey were less likely to have atopic sensitization if they reported having a dog in childhood[18]. In our birth cohort, the southeast Michigan based Childhood Allergy Study, we previously reported that exposure to multiple dogs or cats during the first year of life was associated with a reduced risk for aeroallergen sensitivity at 6–7 years of age[19]. In addition to the effects of pet keeping on attenuating total and allergen-specific IgE, there are many reports suggesting that pets decrease risk for clinically apparent atopy-related disorders including atopic dermatitis[20–22], hayfever[23,24], and asthma[16,17,25,26].

A predictor of elevated cord blood IgE in our study as well as others, is positive family history of atopy and allergic disease[27,28]. This relationship raises a question that is central to the validity of studies that link pet exposure to indicators of atopy: “Does purposeful avoidance of pets in a home contribute to the apparent protective effect of pets on indicators of allergic disease?” When asked directly, 158 (15.1%) of mothers in our study reported avoiding household pets due to concern over potential allergy in family members (although 41 of these mothers reported having a cat or dog in the home during pregnancy). However, excluding these 158 mother-child pairs from our analysis did not affect the association between dog/cat keeping and lower cord IgE levels. Therefore, this seems an unlikely explanation for our findings. A similar lack of effect from excluding similar subjects has been reported by others[13,24]. A recent report directly investigated whether a history of asthma and allergy within families influences pet keeping[29]. The authors found that families with allergy and asthma did not avoid dogs. Although some evidence for cat avoidance was detected they concluded: “Selective avoidance appears to be of limited magnitude and most likely accounts for only a part of the described protective effects of pets on asthma and allergy.”

Although the specific factors mediating immunomodulatory effects of pet keeping remain unknown, a potential mechanism, related to the hygiene hypothesis, is that pets act as vectors for exposure to a variety of microbial products that are produced or carried into the home by the animal. Microbial product exposure appears to trigger immune deviation through stimulation of the innate immune system, shifting the typical skewing of allergic Th2 cytokine responses to allergens in early-life to a Th1 phenotype associated with less IgE production and atopy [30].

Endotoxin, a component of gram negative bacteria has been a substance of intense interest. Initially, investigators linked high endotoxin farming environments to a decreased risk of atopy[31]. Subsequently, a landmark investigation from the cross-sectional Allergy and Endotoxin study (ALEX) in rural Europe reported that those farming environments associated with the highest endotoxin exposure in children were associated with decreased allergic sensitization, hayfever, and atopic asthma[32]. The ALEX investigators also found that exposure to stable environments during pregnancy and during the first year of life was more protective of childhood atopy than subsequent exposure[33].

Both within and outside of farming environments, indoor pets may contribute to endotoxin levels. Several reports link dog and cat ownership to higher household dust endotoxin levels in both rural and metropolitan environments[34–37]. Parallel to our findings with pet ownership, endotoxin in mothers' mattresses is associated with lower cord blood IgE levels[38]. Furthermore, a polymorphism of CD14, a component of the receptor for endotoxin, has been shown to modify the protective effect of dog ownership in infancy on atopic dermatitis suggesting that endotoxin may mediate this protective effect[20]. However, other studies, including our own analysis of mothers in this cohort, have shown that the protective effects of pets and endotoxin are independent of each other[25,39,40]. Nonetheless, a variety of other microbial exposures concomitant with endotoxin appear to stimulate the innate immune system and mediate protective effects on atopic disorders[41]. Finally, and particularly relevant to our study of prenatal exposure, exposure to farming environments with high microbial load during pregnancy is protective against atopic sensitization and associated with upregulated innate immunity in their children[6].

Although highly elevated allergen levels, such as indoor Feld 1 may play a role in dampening allergic senitization to cats via a "modified Th2" mechanism [42–44], this effect appears allergen specific. Therefore, high levels of pet allergen, that are likely to be associated with pet keeping, would not be a plausible explanation for the effect of pet keeping on total cord IgE observed in our study. Indeed, several previous investigations show a positive correlation[38] or no effect[45] of pet allergen levels on IgE at birth.

A limitation of our study is that data that directly links cord blood IgE levels and subsequent clinical allergic outcomes is relatively weak. This may limit the direct clinical relevance of prenatal pet ownership using this imprecise predictor of future allergic disease. However, we believe that separate from its relationship to clinical allergy, cord blood IgE reflects important gene-environment interactions that impact the developing fetus and are operant during this critical period of immune system education. Also, since a clear mechanism explaining the protective effect of pet exposure is still lacking, there is the possibility that pet ownership is an indirect indicator of another unrecognized predictor of atopy such as other social and behavioral characteristics or exposures related to pet keeping that could influence risk.

Recognition of several other limitations is essential to properly interpret our findings. Maternal total and specific IgE levels were measured late in pregnancy, and for some mothers shortly postpartum. However, exclusion of mothers whose blood was obtained postpartum does not significantly influence our results. Also, nearly 17% of the recruited population had to be excluded from these analyses due to missing cord blood measures. Excluded mothers were more likely to deliver preterm babies of low birth weight which may have contributed to difficulty in arranging cord blood collection. In addition, the excluded mothers were slightly older and less likely to have attended college. These differences may limit our ability to extend our conclusions to this population but seem unlikely to have influenced our results. The fact that excluded mothers were less likely to own cats was an unexpected finding that is not clearly explained by interaction with other population characteristics. Finally, our study population is located in a single geographic region in southeast Michigan, potentially limiting our findings to similar local environments and pet-keeping habits.

Our conclusions are strengthened by a diverse general risk prospective cohort study population and analysis of cord blood IgE level as a continuous variable. Previous reports, limited by lower sensitivity assays, analyzed predictors or outcomes associated with early life IgE levels using relatively arbitrary cut points separating high IgE from "normal" levels.

In summary, the presence of indoor dogs or cats during pregnancy is associated with lower cord IgE levels. Our findings confirm existing literature linking animal exposure to alterations in immune development that occurs before birth and that immunomodulatory effects are apparent with common household pet exposure and not exclusively with animals frequently encountered in farming environments. The mechanism by which pets influence immune development remains elusive. However, once identified, the factors mediating this effect will improve our understanding of the natural history of allergic disease and may have therapeutic potential.

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Table I

Demographic and health history information on the mothers of the 1049 participants, WHEALS, Detroit, MI.

Family Characteristics	Entire sample N=1049	Households with at least 1 indoor pet N=375	Households with no pet(s) N=674
Mother's Age			
Mean age in years (SD)	29.3 (5.2)	29.5 (5.0)	29.2 (5.3)
Mother's Ethnicity	n (%)	n (%)	n (%)
African American/Black	658 (62.7%)	167 (44.5%)	491 (72.9%)
Caucasian/White	275 (26.2%)	177 (47.2%)	98 (14.5%)
Other	116 (11.1%)	31 (8.3%)	85 (12.6%)
Mother's Highest Education Level Attained			
Sub-high school	56 (5.3%)	21 (5.6%)	35 (5.2%)
High school	178 (17.0%)	65 (17.3%)	113 (16.8%)
College/tech	524 (50.0%)	165 (44.0%)	359 (53.2%)
Bachelor's degree	194 (18.5%)	78 (20.8%)	116 (17.2%)
Graduate degree	97 (9.2%)	46 (12.3%)	51 (7.6%)
Maternal Smoking during pregnancy			
Yes	126 (12.0%)	59 (15.7%)	67 (9.9%)
No	923 (88.0%)	316 (84.3%)	607 (90.1%)
Baby's sex			
Male	531 (50.6%)	181 (48.3%)	350 (51.9%)
Female	518 (49.4%)	194 (51.7%)	324 (48.1%)
Maternal Self Report of Allergy or Asthma Diagnosis[1]			
Yes	372 (35.7%)	138 (37.0%)	234 (34.9%)
No	671 (64.3%)	235 (63.0%)	436 (65.1%)
Paternal Allergy or Asthma Diagnosis (Reported by mother or father)[2]			
Yes	275 (28.8%)	106 (30.5%)	169 (27.9%)
No	679 (71.2%)	242 (69.5%)	437 (72.1%)
Maternal or Paternal Allergy or Asthma Diagnosis[3]			
Yes	530 (54.4%)	200 (56.0%)	330 (53.5%)
No	444 (45.6%)	157 (44.0%)	287 (46.5%)
Maternal Report of Dog/Cat Allergy[4]			
Yes	277 (26.5%)	98 (26.1%)	179 (26.6%)
No	770 (73.5%)	277 (73.9%)	493 (73.4%)
Maternal Serum Allergen Sensitivity[5]			
Yes	550 (55.5%)	198 (55.5%)	352 (55.5%)
No	441 (44.5%)	159 (44.5%)	282 (44.5%)
Maternal Serum Dog Sensitivity[6]			
Yes	207 (20.8%)	78 (21.8%)	129 (20.3%)

Family Characteristics	Entire sample N=1049	Households with at least 1 indoor pet N=375	Households with no pet(s) N=674
No	786 (79.2%)	279 (78.2%)	507 (79.7%)
Maternal Serum Cat Sensitivity [7]			
Yes	211 (21.3%)	83 (23.3%)	128 (20.1%)
No	781 (78.7%)	273 (76.7%)	508 (79.9%)
Maternal Total serum IgE			
IU/ml, geometric mean (95% CI)	37.1 (33.8, 40.9)	33.6 (28.6, 39.6)	39.3 (35.0, 44.2)
Low birth weight (< 2500 grams) [8]			
Yes	60 (6.1%)	22 (6.3%)	38 (6.0%)
No	923 (93.9%)	329 (93.7%)	594 (94.0%)
Early gestational age (< 37 weeks) [9]			
Yes	74 (7.6%)	27 (7.9%)	47 (7.4%)
No	903 (92.4%)	316 (92.1%)	587 (92.6%)
Indoor Dogs			
Yes	257 (24.5%)	257 (68.5%)	0 (0%)
No	792 (75.5%)	118 (31.5%)	674 (100%)
Indoor Cats			
Yes	179 (17.1%)	179 (47.7%)	0 (0%)
No	870 (82.4%)	196 (52.3%)	674 (100%)

[1] six with missing info

[2] 95 with missing information

[3] 74 with missing information

[4] 2 with missing information

[5] Positive serum allergen sensitivity defined as having a specific IgE ≥0.35 kU/ml for ≥1 of the seven tested aeroallergens, 58 with missing information

[6] 56 with missing information

[7] 57 with missing information

[8] 66 with missing information

[9] 72 with missing information

Table II

Relationship of indoor pet keeping and cord IgE levels compared to no cats or dogs kept indoors during pregnancy, WHEALS, Detroit, MI (units in IU/ml).

	Number of Households (N)	Cord IgE Geometric Mean (95% CI)	Unadjusted Analysis*	Adjusted Analysis†
No dog or cat kept indoors during pregnancy	674	0.34 (0.30, 0.38)	-	-
Either dog(s) or cat(s) kept indoors during pregnancy	375	0.24 (0.20, 0.27)	<0.001	0.025
Only dog(s) kept indoors during pregnancy	196	0.24 (0.19, 0.29)	0.003	0.045
Only cat(s) kept indoors during pregnancy	118	0.21 (0.16, 0.27)	0.001	0.020
Both dog(s) and cat(s) kept indoors during pregnancy	61	0.30 (0.20, 0.44)	0.55	0.56

*linear regression of log transformed IgE values

†Analysis of linear regression models of log transformed IgE values adjusted for ethnicity (classified as African American or non African American)

Table III

Relationship of indoor pet keeping and cord IgE levels compared to no cats or dogs kept indoors during pregnancy, WHEALS, Detroit, MI (units in IU/ml).

	Number of Households (N)	Cord IgE Geometric Mean (95% CI)	Unadjusted Analysis*	Adjusted Analysis†
No dog(s) or cat(s) kept indoors during pregnancy	674	0.34 (0.30, 0.38)	-	-
Indoor dog(s) only				
1 dog, no cats	152	0.25 (0.20, 0.31)	0.021	0.17
2 or more dogs, no cats	44	0.20 (0.13, 0.31)	0.016	0.051
Indoor cats only				
1 cat, no dogs	75	0.22 (0.16, 0.31)	0.020	0.063
2 or more cats, no dogs	43	0.18 (0.12, 0.29)	0.007	0.11
Indoor dog(s) and cat(s)				
1 or more dogs plus 1 or more cats kept indoors during pregnancy	61	0.30 (0.20, 0.44)	0.55	0.56

*linear regression of log transformed IgE values

†adjusted for AA vs non-AA race