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Effect of Prenatal Dog Exposure on Eczema Development in Early and Late Childhood

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Dog Exposure; Eczema; Prenatal exposure; Atopic March

Eczema in early childhood, often the start of the “atopic march”, increases the likelihood of developing subsequent atopic conditions (food allergy, allergic asthma, and allergic rhinitis)[1, 2]. Modifiable environmental risk factors, important to eczema pathogenesis, may represent potential interventions. Studies demonstrate protective effects of domestic pets on eczema development[3, 4]. Previous reports focus on eczema in early childhood but do not address potential effects in late childhood[3, 4]. This study compares the associations of prenatal and first-year dog exposure to eczema in early childhood (age 2 years) and late childhood (age 10 years) in the Wayne County Health, Environment, Allergy and Asthma Longitudinal study (WHEALS), a racially and socioeconomically diverse birth cohort. We also assessed whether prenatal dog exposure is associated with persistence or resolution of eczema from age 2 to 10 years and whether dogs are associated with atopic and non-atopic eczema.

WHEALS enrolled pregnant women (21–49 years) due September 2003-December 2007 residing in the metro-Detroit area. Participants provided informed consent, and study protocols were approved by the Henry Ford Health (HFH) Institutional Review Board[5]. Our analysis included maternal-child pairs who completed a prenatal interview and had eczema history evaluated by a physician during study clinic visits at age 2 and/or 10 years (N=794; Figure E1). Using patient history and physical examination, physicians assessed each child’s history of eczema over time. “Early eczema only” refers to eczema diagnosis prior to or at age 2, but no eczema at age 10. “Late eczema only” refers to current eczema diagnosis at age 10, but not ≤2 years. “Persistent eczema” refers to eczema diagnosis at age

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≤2 years with eczema present at age 10; if absent at age 10, the child is classified as having "Resolved eczema". Prenatal dog exposure was defined as ≥1 indoor dogs in the home for ≥1 hour per day during pregnancy, for at least one week. Median dog exposure was beyond pregnancy at 24 months (IQR=10 to 69 months). Dogs in the first year of life was defined similarly. Serum allergen-specific IgE (sIgE) was measured for 10 common inhalant/food allergens at age 2 (*Dermatophagoides farinae*, ragweed, *Alternaria alternatum*, dog, cat, grass, cockroach, egg, milk, and peanut) and 11 allergens at age 10 (dog, cat, cockroach, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, ragweed, grass, mold mixture, egg, peanut, and milk). Atopy was defined as sIgE≥0.35 IU/mL to ≥1 allergens. Eczema was further refined as atopic eczema (early atopic eczema: early eczema and atopic at age 2, late atopic eczema: late eczema and atopic at age 10, persistent atopic eczema: persistent eczema and atopic at 2 or 10). Non-atopic eczema was defined similarly.

Logistic regression was used to determine association between dog-keeping and childhood eczema, with main effect p-values<0.05 considered significant. Interaction terms were included to test *a priori* hypothesized effect modification (maternal eczema, maternal race, mode of delivery, first born child, and prenatal environmental tobacco smoke [ETS] exposure), with interaction p-values <0.10 considered significant. Models were refit after adjusting for potential confounders (*a priori* hypothesized as associated with dogs and eczema), with confounding indicated by effect size change >20%.

Rate of indoor dog keeping was 26% prenatally, and rates of eczema at ages 2 and 10 were 22% and 21%, respectively (Table 1). Among children with known eczema status at both time points (N=394), 14% had "Early eczema only", 11% had "Late eczema only", and 11% had "Persistent eczema" (Table 1). In multivariable analyses, children with prenatal dog exposure had lower odds of "Early eczema only" (aOR[95% CI] = 0.28[0.09, 0.83], p=0.022, Table 2). This association was weaker and not statistically significant for "Late eczema only" (aOR[95% CI] = 1.36[0.63,2.92], p=0.433, Table 2), and did not reach statistical significance for "Persistent eczema" after adjustment (aOR[95% CI] = 0.32[0.10, 1.02], p=0.053, Table 2). We then examined the impact of effect modifiers. Mode of delivery significantly modified the effect of dogs in the first year of life on early eczema development (interaction p=0.056). Specifically, an effect was observed only among vaginally delivered children (OR[95% CI]=0.07 [0.01, 0.54], p=0.011), but not among children delivered via C-section (OR [95% CI]=0.68 [0.22, 2.12], p=0.51); all other interaction p-values were≥0.10.

Previous studies reveal associations between prenatal and early life dog exposures with prevention of early childhood eczema[3, 4, 6]. Our study confirms this, with protective effects on early, but not late childhood, and strongest effect among children delivered vaginally. Though the effect size appeared larger for early non-atopic eczema than early atopic eczema, we were limited in sample size to fully elucidate these differences. Prenatal dog effect on persistent eczema failed to reach significance after covariate adjustment. However, the effect size was strong (OR=0.32) and warrants further exploration in larger studies.

Dogs may provide exposure to microbial diversity beneficial to immune development[7], and alterations may influence the immunological mediators leading to atopic conditions[6, 7]. The first year of life is potentially the critical window[6]. Our results suggest that *in utero*

exposure may prevent early eczema. Most households with dogs during pregnancy keep their pets during infancy, making effects difficult to disentangle. Study strengths include its prospective nature, large sample size, and representing a racially and socioeconomically diverse population. We accounted for potentially modifiable factors which did not modify the overall effect except for delivery mode. The lack of significant interactions could be due to insufficient sample size. Some biases may include loss to follow-up, potentially biasing effect estimates. Parents with allergic diseases may avoid domestic animal exposure, which could result in reverse causation. Due to limited data, we considered maternal rather than paternal eczema. Our eczema prevalence is higher than previous reports[8]. However, eczema is reportedly more common in African Americans[9].

In summary, our data suggest that prenatal and early life dog exposure has a significant protective effect on eczema development at or before age 2. Since pet-keeping influences infant gut microbial composition[7], the lower rate of eczema in dog-exposed children may be linked to altered early-life immune development triggered by microbial exposures. Clinically, our findings suggest that prenatal dog exposure could protect against early eczema.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Clinical Implications:

Dog exposure is protective in early eczema development, but effects in late childhood are unknown. We find prenatal and first year dog exposure has a significant protective effect on early eczema development by age 2.

Table 1:

Descriptive characteristics of children with known AD status at age 2 or age 10 (N=794)

Variable	Level	N = 794	%
Mom Eczema (ever in lifetime)	No	590	74.7
	Yes	200	25.3
Maternal Race	White	199	25.1
	African American	471	59.3
	Hispanic	47	5.9
	Arabic	41	5.2
	Other/Mixed Race	36	4.5
Mode of Delivery	Vaginal	496	62.6
	C-Section	296	37.4
First Born Child	No	495	62.3
	Yes	299	37.7
Prenatal Indoor Dog(s)	No	587	73.9
	Yes	207	26.1
Indoor Dog(s) in First Year of Life	No	444	69.6
	Yes	194	30.4
Prenatal Indoor Cat(s)	No	657	82.8
	Yes	137	17.2
Prenatal ETS Exposure	No	609	76.7
	Yes	185	23.3
Eczema Category	Never	255	64.7
	Early[1]	54	13.7
	Late[2]	43	10.9
	Persistent[3]	42	10.7
Atopic at Age 2	No	251	48.5
	Yes	266	51.5
Total IgE at Age 2	Geometric Mean (SD)	21.1 (4.2)	
Atopic at Age 10	No	226	41.9
	Yes	314	58.2
Total IgE at Age 10	Geometric Mean (SD)	68.7 (4.9)	

[1] N=21 with early atopic eczema, N=18 with early non-atopic eczema, N=15 with missing atopy status

[2] N=31 late atopic eczema, N=12 late non-atopic eczema

[3] N=34 persistent atopic eczema, N=3 persistent non-atopic eczema, N=5 with missing atopy status

Table 2:

Association between dog exposure and eczema from ages 2 to 10.

Exposure	Outcome	Unadjusted			Adjusted		
		N	OR (95% CI)	p-value	N	OR (95% CI)	p-value
Prenatal Dog Exposure	Early Only vs. Never Eczema	309	0.32 (0.14, 0.74)	0.008	240	0.28 (0.09, 0.83)[1]	0.022
	Early Atopic vs. Never Eczema	276	0.36 (0.1, 1.25)	0.107	220	0.48 (0.13, 1.81)[1]	0.277
	Early Non-Atopic vs. Never Eczema	273	0.13 (0.02, 0.97)	0.046	217	N/A[1,2]	N/A[1,2]
	Late Only vs. Never Eczema	298	0.93 (0.46, 1.88)	0.842	294	1.36 (0.63, 2.92)[3]	0.433
	Late Atopic vs. Never Eczema	286	1.02 (0.46, 2.27)	0.955	282	2.14 (0.84, 5.46)[3]	0.111
	Late Non-Atopic vs. Never Eczema	267	0.72 (0.19, 2.72)	0.624	263	0.47 (0.11, 2.07)[3]	0.321
	Persistent vs. Never Eczema	297	0.36 (0.15, 0.88)	0.026	230	0.32 (0.10, 1.02)[1]	0.053
	Persistent Atopic vs. Never Eczema	289	0.46 (0.18, 1.16)	0.098	225	0.41 (0.12, 1.37)[1]	0.148
	Persistent Non-Atopic vs. Never Eczema	258	N/A[2]	N/A[2]	202	N/A[1,2]	N/A[1,2]
	Resolved Eczema: Yes vs. No	96	0.89 (0.28, 2.89)	0.851	72	1.08 (0.21, 5.54)[1]	0.93
Dog Exposure in the First Year of Life	Early Only vs. Never Eczema	266	0.28 (0.11, 0.69)	0.006	211	0.22 (0.06, 0.78)[1]	0.019
	Early Atopic vs. Never Eczema	239	0.21 (0.05, 0.94)	0.042	195	0.33 (0.07, 1.55)[1]	0.16
	Early Non-Atopic vs. Never Eczema	234	0.14 (0.02, 1.06)	0.057	190	N/A[1,2]	N/A[1,2]
	Late Only vs. Never Eczema	257	1.00 (0.48, 2.06)	0.997	255	1.31 (0.60, 2.87)[3]	0.503
	Late Atopic vs. Never Eczema	246	1.13 (0.49, 2.59)	0.774	244	1.95 (0.74, 5.15)[3]	0.177
	Late Non-Atopic vs. Never Eczema	230	0.72 (0.19, 2.79)	0.635	228	0.6 (0.15, 2.51)[3]	0.488
	Persistent vs. Never Eczema	253	0.50 (0.21, 1.20)	0.119	200	0.45 (0.14, 1.47)[1]	0.187
	Persistent Atopic vs. Never Eczema	247	0.64 (0.26, 1.57)	0.331	196	0.61 (0.18, 2.08)[1]	0.428
	Persistent Non-Atopic vs. Never Eczema	221	N/A[2]	N/A[2]	177	N/A[1,2]	N/A[1,2]
	Resolved Eczema: Yes vs. No	81	0.56 (0.17, 1.86)	0.348	61	0.64 (0.10, 3.98)[1]	0.628

[1]Adjusted for maternal race, mode of delivery, prenatal indoor cats, and log(total IgE at age 2).

[2]Model did not converge.

[3]Adjusted for maternal race, mode of delivery, prenatal indoor cats, and log(total IgE at age 10).