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Maternal interpersonal trauma and cord blood IgE levels in an inner-city cohort: A life-course perspective

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Background: Prenatal stress affects immunocompetence in offspring, although the underlying mechanisms are not well understood.

Objective: We sought to examine associations between maternal lifetime interpersonal trauma (IPT) and cord blood total IgE levels in a sample of urban newborns (n = 478).

Methods: Maternal IPT during childhood and adolescence (birth to 17 years), adulthood (18 years to index pregnancy), and the index pregnancy were ascertained by using the Revised Conflict Tactics Scale at 28.4 ± 7.9 weeks' gestation. Cord blood IgE levels were derived by using a fluoroenzyme immunoassay. We examined effects of maternal IPT on increased cord blood IgE levels (upper quartile, 1.08 IU/mL) by using logistic regression, adjusting for confounders and mediating variables.

Results: Maternal trauma was categorized as unexposed (n = 285 [60%]), early (childhood and/or teenage years only, n = 107 [22%]), late (adulthood and/or index pregnancy only, n = 29 [6%]), and chronic (early and late, n = 57 [12%]) exposure. Relative to no IPT, early (odds ratio [OR], 1.78; 95% CI, 1.05-3.00) and chronic maternal IPT (OR, 2.25; 95% CI, 1.19-4.24) were independently associated with increased IgE levels in unadjusted analyses. When adjusting for standard controls, including maternal age and race, season of birth, child's sex, and childhood and current socioeconomic status, early effects became nonsignificant (OR, 1.48; 95% CI, 0.85-2.58). Chronic exposure remained significant in fully adjusted models, including standard controls, current negative life events, allergen exposure, and potential pathway variables (maternal atopy, prenatal smoking, and birth weight; OR, 2.18; 95% CI, 1.06-4.50).

Conclusion: These data link chronic trauma over the mother's life course with increased IgE levels in infants at birth. Research examining associations between maternal trauma and indicators of offspring's atopic risk might be particularly relevant in inner-city high-risk populations. (J Allergy Clin Immunol 2009;124:954-60.)

Key words: *Interpersonal trauma, life course, pregnancy, cord blood IgE, urban asthma*

Hypersensitivity to environmental stimuli associated with IgE production is a fundamental feature of atopy, predisposing individuals to clinical disorders, including allergic rhinitis, atopic dermatitis, and allergic asthma.[1] Evidence linking psychologic stress to allergy and asthma[2] suggests that the association is mediated through effects on neuroimmunoregulatory processes that set the stage for altered immune reactivity and enhanced IgE production.[3] Examining relationships between stress exposure during critical developmental periods and biomarkers of immune response that precede clinical disease might elucidate pathways that increase vulnerability to atopy in response to stress.

Immune development and the predisposition to atopy begin during gestation.[1,3] Increased cord blood IgE levels are an early indicator of immune polarization toward an atopic phenotype associated with the development of allergic diseases in later childhood.[4] Prospective studies demonstrate that increased IgE levels detected during infancy track with age.[5,6]

Maternal stress influences fetal programming of physiologic systems (eg, immune function); consequently, stress effects might be transgenerational.[3] Prenatal stress might disrupt maternal physiology (the hypothalamic-pituitary-adrenal [HPA] axis and the sympathetic-adrenal-medullary system), which, in turn, upregulates maternal and fetoplacental T_H2 cytokine production. The enhanced T_H2 cytokine/chemokine milieu might affect fetal immune function, including IgE isotype development.[3] Thus infants exposed to maternal stress *in utero* might be more likely to express increased IgE levels at birth. Because interpersonal trauma (IPT) is more likely to result in lasting biobehavioral sequelae (eg, neurohormonal disruption)[7] and intergenerational effects compared with other stressors,[8] maternal trauma might be a particularly potent inducer of immunomodulatory effects starting *in utero*.[9] Moreover, such stressors disproportionally burden urban, lower-income US populations,[10] who are also overly burdened by allergic disorders.

Although studies of maternal stress and infant outcomes typically examine events occurring during pregnancy,[11] we consider IPT across the mother's life course. The life-course

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Abbreviations used
HPA: Hypothalamic-pituitary-adrenal
IPT: Interpersonal trauma
NLE: Negative life event
OR: Odds ratio
R-CTS: Revised Conflict Tactics Scale
SES: Socioeconomic status
WIC: Women, Infants, and Children

perspective posits that some stressors might influence health through 2 mechanisms, early programming and cumulative pathways, in addition to more immediate effects.[12] Early programming can occur if exposures during sensitive developmental periods have lasting psychobiologic sequelae. Both early childhood and adolescence have been identified as sensitive periods susceptible to the effects of stress.[3,13] Exposure to IPT in earlier life can generate disrupted physiologic stress responses even several years after the trauma.[14,15] Thus maternal IPT might be linked to infant health through more latent effects (ie, lasting effects from abuse in childhood/adolescence), proximate effects (ie, trauma experienced in or around the pregnancy), and cumulative life-course effects (ie, allostatic load of accumulated traumas over the mother's life).[15,16] No human studies have examined the influence of maternal trauma on the expression of atopic phenotypes at birth.

We investigated the relationship between maternal IPT experienced over her life course and cord blood total IgE levels, a biomarker of atopic risk at birth, in an urban population-based study. We hypothesized that infants born to mothers with chronic trauma exposure (ie, both early in life and more proximate to the pregnancy) would be at greatest risk of expressing increased IgE levels.

METHODS

Participants

Participants were from the Asthma Coalition on Community, Environment, and Social Stress project, a prospective cohort originally funded to recruit 500 pregnant women and their children to study the effects of prenatal maternal and early-life stress on urban childhood asthma risk, as described elsewhere.[17] Briefly, English- or Spanish-speaking pregnant women who were at least 18 years old and receiving prenatal care at Brigham & Women's Hospital, Boston Medical Center, 3 metropolitan Boston community health centers, and their associated Women, Infants, and Children (WIC) programs were recruited between August 2002 and January 2007. Research assistants approached women receiving prenatal care on selected clinic days, of whom 78.1% were eligible and agreed to enroll. Those who chose not to participate answered a screener questionnaire including race/ethnicity, education, and annual household income; no significant differences in these covariates emerged between the participants and those who declined. The study was approved by the human studies committees at the Brigham & Women's Hospital and Boston Medical Center; written informed consent was obtained in the subject's primary language (English or Spanish). Cord blood IgE levels and complete data on maternal IPT were available for 478 dyads. Comparison of children with and without IgE measurement showed no differences based on sociodemographics or maternal trauma exposure.

Measures and procedures

Baseline questionnaire data were obtained at 28.4 ± 7.9 weeks' gestation.

IPT. Mothers completed the Revised Conflict Tactics Scale (R-CTS) short form, which has previously documented reliability and validity.[18] IPT was assessed during childhood (≤11 years of age), adolescence (12-17 years of age), adulthood before the current pregnancy, and during the pregnancy. For each life stage, exposure was assessed by using the same 6 items, asking mothers whether anyone had ever pushed, grabbed, or shoved them; kicked, bit, or punched them; hit them with something that hurt their body; choked or burned them; forced them to have sexual activities; or physically attacked them in some other way. For the childhood period, the stem to the question was modified to ask, "Did anyone at least 5 years older than you ever…" followed by the items. Mothers were classified as exposed in each life period if they answered yes to any of the items.

Life-course IPT was categorized as (1) unexposed, (2) early (during childhood or teenage years only), (3) late (during adulthood and/or the index pregnancy only), or (4) chronic (both early and late) exposure. Relatively small numbers reported abuse only in childhood (n = 42) or adolescence (n = 32), and 61% of women experiencing IPT in adolescence also reported earlier childhood exposure; these categories were collapsed. Pregnancy and adulthood periods were also combined given the small number reporting abuse during pregnancy (n = 21) and the high covariance between the 2 periods (67% experiencing IPT during pregnancy also reported exposure in adulthood before the pregnancy).

Maternal and cord blood IgE levels. Sera from mothers collected during pregnancy and venous placental cord blood collected at birth were analyzed with the CAP fluorescent enzyme immunoassay (Pharmacia [now Phadia], Uppsala, Sweden) for total IgE levels (in international units per milliliter). A modified protocol was used for cord blood, reducing the lower limit of detection from 2.0 to 0.2 IU/mL.[19] Maternal IgE levels, which were available for 320 mothers, were considered a control variable in secondary sensitivity analyses detailed below.

Covariates. All analyses were adjusted for the child's sex and season of birth, given documented associations with cord blood IgE levels.[20] Potential confounders included younger maternal age, low socioeconomic status (SES), and minority status, which are associated with IPT and asthma/atopy in both mothers and infants.[9] Thus standard controls included maternal age, race/ethnicity, and education. The mother's current SES was further controlled through a 3-item index of economic difficulties.[21] Items were scored on a 5-point scale and summed; higher scores indicated greater difficulties (range, 0-15). Lower childhood SES is linked to increased abuse risk[22] and asthma risk in the mothers,[23] and both can influence atopic susceptibility in the next generation. Each mother reported whether her parents owned their home during her childhood. A binary indicator of parental home ownership over the mother's childhood (ages 0-20 years) was included as a marker of childhood socioeconomic circumstances.[24-26] Women experiencing IPT during pregnancy are more likely to report other adverse events.[27] Using the 63-item Crisis in Family Systems-Revised, which has been validated in English and Spanish,[28,29] participants indicated whether they experienced events spanning several domains (community violence/safety and housing issues) during the pregnancy and rated endorsed events as positive, negative, or neutral. Items related to IPT were omitted because the R-CTS assessed these exposures. A summary score based on the total events rated negative was calculated (current negative life events [NLEs]). Lower-SES populations disproportionately exposed to IPT might also live in poor housing with increased exposure to atopy-exacerbating environmental factors (eg, indoor allergens[30]). Settled dust was collected during pregnancy from the mother's bed and bedroom floor by using a standardized protocol.[31] Dust mite (Der f 1 and Der p 1) and cockroach (Bla g 1 and Bla g 2) allergens were measured with an mAb ELISA (Indoor Biotechnologies, Charlottesville, Va). Exposure was defined as previously described (ie, Der f 1 and Der p 1, >0.20 μg/g; Bla g 1 and Bla g 2, >2 U/g).[32]

Finally, we assessed potential pathways through which maternal trauma history might contribute to newborn IgE expression. IPT is associated with risk factors previously correlated with offspring's atopy or cord blood IgE levels, including preterm delivery and low birth weight[33,34] and smoking.[35] Thus we adjusted for a continuous measure of birth weight for gestational age[36] and for maternal prenatal smoking based on self-report using timeline follow-back procedures.[37] Women exposed to IPT in earlier life might themselves be at increased risk of asthma/atopy, and maternal atopy predicts increased cord blood IgE levels. Maternal atopy was defined as a clinician-based lifetime diagnosis of asthma, hay fever, and/or eczema.

Statistical analysis

All analyses used SAS statistical software version 9 (SAS Institute, Inc, Cary, NC). Cord blood and maternal IgE levels were log transformed because of skewness, assigning a value of 0.10 to undetectable values. The association between the mean of log cord blood IgE levels and trauma exposure categories was not significant. Cord blood levels were *a priori* divided into quartiles, with serum levels at or greater than the upper 25% (1.08 IU/mL) considered high. This value approximates levels in prior studies demonstrating associations between more extremely increased cord blood IgE levels and increased atopic risk in later childhood.[38-40] Categorization also makes the decision of the value to define the nondetectable values as irrelevant and can model a nonlinear or threshold relationship between IPT and IgE levels.

Relationships between IPT and covariates and between cord blood IgE levels and covariates were examined by using Kruskal-Wallis ANOVA to test differences in means for multiple groups and the Pearson χ^2 statistic to test differences in proportions. Bonferroni tests and Wilcoxon rank sum testing were conducted for each 2-group pairing within multigroup comparisons. Logistic regressions predicted increased cord blood IgE levels. We first fit a univariate model including only IPT. We next added control variables, followed by NLEs and home allergen exposure. The final model included hypothesized pathway variables. Results are presented as odds ratios (ORs), with 95% CIs in parentheses.

In secondary analysis with a reduced sample, we further adjusted for prenatal maternal total IgE levels.[41] Analyses were also run with different IgE cutoff points to examine sensitivity to alternative specifications.

RESULTS

Tables I and II describe sample characteristics stratified by periods of IPT over the mother's life course and by IgE categories, respectively. Overall maternal age was 26.6 ± 5.7 years. The sample was largely Hispanic (59%) or black (30%, Table I). More respondents experienced no IPT than early (60% vs 22%, $P < .001$), late (60% vs 6%, $P < .001$), or chronic (60% vs 12%, $P < 0.001$) IPT. More Hispanics relative to blacks or other/mixed race subjects reported no IPT (66% vs 52% [$P < .003$] and 49% [$P < .03$], respectively); a higher proportion of blacks reported early-life IPT than Hispanics (31% vs 17%, $P < .001$). More atopic mothers reported chronic abuse than nonatopic mothers (16.5% vs 9%, $P < .02$). Mothers with chronic IPT reported more frequent NLEs compared with unexposed mothers (4.2 ± 3.92 vs 1.7 ± 2.3, $P < .001$), those with early exposure (4.2 ± 3.92 vs 2.8 ± 2.7, $P < .001$), and those with later-life exposure only (4.2 ± 3.92 vs 2.1 ± 2.4, $P < .001$). Current economic difficulties were higher for late-life exposure compared with no exposure (6.4 ± 2.8 vs 5.4 ± 2.3, $P < .03$), chronic versus no exposure (6.7 ± 2.7 vs 5.4 ± 2.3, $P < .001$), and chronic compared with early exposure (6.7 ± 2.7 vs 5.8 ± 2.6, $P < .03$). No significant differences emerged across IPT groups based on parental home ownership, maternal education, child's sex, birth weight, maternal age, household allergen exposure, or season of birth. Prenatal smoking prevalence for mothers reporting chronic IPT (23%) was more than double that of mothers reporting no exposure (11%), early IPT (11%), and late IPT (10%), although these differences were not significant.

More blacks than Hispanics had increased cord blood IgE levels (n = 45 [32%] vs n = 58 [21%], $P < .01$), as did offspring of atopic versus nonatopic mothers (n = 55 [32%] vs n = 65 [21%], $P < .00$) and infants whose mothers reported their family not owning their home during her childhood versus those reporting parental home ownership (n = 61 [35%] vs n = 45 [18%], $P < .01$; Table II).

No significant differences emerged between trauma exposure groups in terms of IgE geometric means ($P = .28$, Table III). However, among the women experiencing IPT during any life period, there was increased prevalence of more extreme levels of cord blood IgE (indexed as ≥1.08 IU/mL; early life, 30% [$P < .03$], late life, 35% [$P < .04$], chronic IPT, 35% [$P < .01$]; all relative to no IPT, 20%).

The ORs (95% CIs) of increased cord blood IgE levels by mother's IPT exposure categories, when considered simultaneously, are presented in Table IV. Early IPT (OR, 1.78; 95% CI, 1.05-3.00) and chronic exposure (early and late; OR, 2.25; 95% CI, 1.19-4.24) were independently associated with increased IgE levels in unadjusted analysis; later-life trauma was borderline significant. Adjusting for sociodemographics and season of birth (model 1) attenuated the effects for early IPT to nonsignificance. Stepwise analyses adding in sociodemographic indicators one at a time and in pairs (not shown) revealed that race/ethnicity and home ownership (OR for early IPT, 1.51; 95% CI, 0.88-2.60) accounted for the attenuation of early IPT effects. The effect estimate for chronic exposure to IPT was not changed in magnitude or precision (ie, confidence bounds were unchanged), even with inclusion of posited pathway variables (ie, birth weight for gestational age, maternal atopy, and prenatal smoking).

When adjusting for all covariates plus maternal IgE levels, the association between maternal IPT and cord blood IgE levels remained (OR for early IPT, 1.43 [95% CI, 0.66-3.10]; OR for late IPT, 3.26 [95% CI, 1.07-9.96]; and OR for chronic IPT, 2.92 [95% CI, 1.22-6.96). There was also a significant independent effect of maternal IgE level (per 1-unit increase in log maternal IgE level; OR, 1.72; 95% CI, 1.35-2.18). We also considered alternative IgE cutoffs for the top 20% and 33% to examine sensitivity to alternative specifications. When a more extreme (top 20%) cutoff for high IgE level was used (1.40 IU/mL), the effects increased [OR for early IPT, 1.80 [95% CI, 0.98-3.31]; OR for late IPT, 2.47 [95% CI, 0.93-6.51]; and OR for chronic IPT, 2.25 [95% CI, 1.03-4.91]) in fully adjusted models. When using a cutoff below levels previously linked with atopic clinical disorders in children (ie, upper tertile for IgE [0.79 IU/mL]), there was no longer significance (ORs were 1.35 [95% CI, 0.80-2.29], 1.86 [95% CI, 0.79-4.39], and 1.51 [95% CI, 0.76-3.02] for early, late, and chronic IPT, respectively).

DISCUSSION

These analyses provide the first suggestion that chronic exposure to IPT across the mother's life course is associated with increased IgE levels in newborns when adjusted for race/ethnicity, childhood and current SES, other current NLEs, household allergens, season of birth, and potential mediators (eg, prenatal smoking, birth weight for gestational age, maternal atopy and IgE level). Although results are most consistent with cumulative life-course effects in the mother potentiating the child's immune response toward IgE production, there is some support for independent effects of exposure during early life, when these mothers might be more vulnerable to lasting programming effects of stress (childhood and adolescence).[3,13] Finally, our analyses did not suggest that birth weight for gestational age, maternal smoking, or maternal atopy operated as mediators.

In general, physiologic systems operate at higher or lower levels than in normal homeostasis in response to stress. Immune and neural defensive biologic responses important for short-term reaction to stress might produce long-term damage if not checked and terminated. Such chronic stress effects have been conceptualized as "allostatic load." Accumulated experiences of IPT across the mother's life might result in such accommodation with

TABLE I. Distribution of covariates across IPT exposure categories over the mother's life course (n = 478)

		Periods of IPT				
	All, n = 478	**No IPT, n = 285 (60%)**	**Early-life IPT, n = 107 (22%)**	**Late-life IPT, n = 29 (6%)**	**Chronic IPT, n = 57 (12%)**	***P* value***
Maternal age (y), mean ± SD	26.6 ± 5.7	26.4 ± 5.6	26.1 ± 6.0	27.2 ± 4.9	27.7 ± 6.1	.31
Maternal race, no. (%)						.001
Hispanic	282 (59%)	188 (66%)	49 (46%)	17 (58%)	28 (49%)	
Black	141 (30%)	73 (26%)	44 (41%)	6 (21%)	18 (32%)	
White	20 (4%)	7 (2%)	7 (6.5%)	2 (7%)	4 (7%)	
Other/mixed	35 (7%)	17 (6%)	7 (6.5%)	4 (14%)	7 (12%)	
Maternal education, no. (%)						.66
< High school	165 (35%)	101 (35%)	37 (34%)	10 (34%)	17 (30%)	
High school degree	140 (29%)	80 (28%)	34 (32%)	6 (21%)	20 (35%)	
≥ Some college	144 (30%)	84 (30%)	31 (29%)	13 (45%)	16 (28%)	
Missing	29 (6%)	20 (7%)	5 (5%)	0 (0%)	4 (7%)	
Current economic difficulties, mean ± SD	5.7 ± 2.5	5.4 ± 2.3	5.8 ± 2.6	6.4 ± 2.8	6.7 ± 2.7	.002
Prenatal smoking, no. (%)						.12
Prenatal smoking	60 (13%)	32 (11%)	12 (11%)	3 (10%)	13 (23%)	
No smoking	407 (85%)	244 (86%)	93 (87%)	26 (90%)	44 (77%)	
Missing	11 (2%)	9 (3%)	2 (2%)	0 (0%)	0 (0%)	
Maternal atopy, no. (%)						.04
Atopy	170 (36%)	88 (31%)	42 (39%)	12 (41%)	28 (49%)	
No atopy	308 (64%)	197 (69%)	65 (61%)	17 (59%)	29 (51%)	
Parental home ownership, no. (%)						.25
Parents owned home	248 (52%)	152 (53%)	51 (47%)	16 (55%)	29 (51%)	
Parents did not own home	175 (37%)	94 (33%)	50 (47%)	9 (31%)	22 (38.5%)	
Missing	55 (11%)	39 (14%)	6 (6%)	4 (14%)	6 (10.5%)	
Child's sex, no. (%)						.75
Male	250 (52%)	147 (52%)	58 (54%)	13 (45%)	32 (56%)	
Female	228 (48%)	138 (48%)	49 (46%)	16 (55%)	25 (44%)	
Birth weight, *z* value for gestational age, mean ± SD	−0.4 ± 0.2	−0.5 ± 1.2	−0.3 ± 1.3	−0.3 ± 1.1	−0.5 ± 1.2	.75
Season of birth, no. (%)						.82
Winter	135 (28%)	78 (27%)	36 (34%)	7 (24%)	14 (25%)	
Summer	100 (21%)	62 (22%)	20 (19%)	7 (24%)	11 (19%)	
Spring	117 (25%)	67 (24%)	25 (23%)	6 (21%)	19 (33%)	
Fall	126 (26%)	78 (27%)	26 (24%)	9 (31%)	13 (23%)	
Other current NLEs,† mean ± SD	2.3 ± 2.8	1.7 ± 2.3	2.8 ± 2.7	2.1 ± 2.4	4.2 ± 3.9	.001
Detectable dust mite‡ in home, no. (%)						.74
Dust mite	345 (73%)	71 (25%)	24 (23%)	10 (35%)	17 (30%)	
No dust mite	88 (18%)	184 (65%)	71 (66%)	19 (65%)	37 (65%)	
Missing dust mite	45 (9%)	30 (10%)	12 (11%)	0 (0%)	3 (5%)	
Detectable cockroach§ in home, no. (%)						.08
Cockroach	122 (26%)	194 (68%)	83 (78%)	22 (76%)	46 (81%)	
No cockroach	311 (65%)	61 (21%)	12 (11%)	7 (24%)	8 (14%)	
Missing cockroach	45 (9%)	30 (11%)	12 (11%)	0 (0%)	3 (5%)	

*For differences between nonmissing multigroup comparisons using ANOVA and χ^2 distribution.
†Current NLEs other than IPT.
‡Detectable levels for dust mites (Der f 1 and Der p 1, >0.02 μg/g).
§Detectable levels for cockroach allergens (Bla g 1, >0.40 U/g; Bla g 2, >1.0 U/g).

disturbed regulation of the maternal stress systems (eg, HPA axis and sympathetic-adrenal-medullary system), which might, during pregnancy, influence fetal immune development.[8,42] The fetal HPA axis can be stimulated to amplify fetal glucocorticoid excess, as well as to activate additional elements of the fetal stress response (ie, catecholamines) affecting the developing immune system. Alterations in stress-induced maternal cortisol levels might also influence T_H2 cell predominance, perhaps through its influence on cytokine production.[3] This might induce an enhanced shift toward T_H2-mediated humoral immunity and IgE production. Although these *in utero* responses might be adaptive in the short-term and geared toward coping with anticipated environmental challenges, ultimately they might exact a toll, contributing to increased risk of atopic diseases in later life.

Effects of childhood adversity might operate directly through latent programming effects or more indirectly through an increased likelihood of adult NLE exposure, as well as enhanced life-stress sensitivity, the so-called stress sensitization model.[43] In models adjusting for later-life exposure, as well as chronic exposure, the mother's early-life experience of IPT was significantly associated with increased cord blood IgE levels. That this attenuated when adding race/ethnicity, childhood SES, or both is interesting. We saw in the descriptive analysis that blacks were more likely to report early-life abuse, which might have contributed to the attenuation. Higher childhood SES has been associated with more positive caregiving and less family chaos, which might buffer the adverse effects of early childhood adversity. In accordance with this hypothesis, recent analyses conducted in the Fragile Families and Child

TABLE II. Distribution of covariates across IgE categories (n = 478)

	IgE level categories		
	Low, n = 358 (75%)	High, n = 120 (25%)	*P* value*
Maternal age (y), mean ± SD	27 ± 5.7	26 ± 5.7	.03
Maternal race, no. (%)			.05
Hispanic	224 (62%)	58 (48%)	
Black	96 (27%)	45 (38%)	
White	13 (4%)	7 (6%)	
Other/mixed	25 (7%)	10 (8%)	
Maternal education, no. (%)			.23
< High school	131 (37%)	34 (28%)	
High school degree	100 (28%)	40 (33%)	
≥ Some college	105 (29%)	39 (33%)	
Missing	22 (6%)	7 (6%)	
Current economic difficulties, mean ± SD	5.6 ± 2.4	6.1 ± 2.7	.04
Prenatal smoking, no. (%)			.12
Prenatal smoking	46 (13%)	14 (12%)	
No smoking	304 (85%)	103 (86%)	
Missing	8 (2%)	3 (2%)	
Maternal atopy, no. (%)			.01
Atopy	115 (32%)	55 (46%)	
No atopy	243 (68%)	65 (54%)	
Parental home ownership, no. (%)			.001
Parents owned home	203 (57%)	45 (37%)	
Parents did not own home	114 (32%)	61 (51%)	
Missing	41 (11%)	14 (12%)	
Child's sex, no. (%)			.49
Male	184 (51%)	66 (55%)	
Female	174 (49%)	54 (45%)	
Birth weight, *z* value for gestational age, mean ± SD	−0.4 ± 1.2	−0.4 ± 1.3	.72
Season of birth, no. (%)			.45
Winter	95 (27%)	40 (33%)	
Summer	79 (22%)	21 (17%)	
Spring	90 (25%)	27 (23%)	
Fall	94 (26%)	32 (27%)	
Other Current NLEs,† mean ± SD	2.2 ± 2.6	2.5 ± 3.1	.35
Detectable dust mite‡ in home, no. (%)			.97
Dust mite	235 (66%)	76 (63%)	
No dust mite	92 (26%)	30 (25%)	
Missing dust mite	31 (8%)	14 (12%)	
Detectable cockroach§ in home, no. (%)			.12
Cockroach	72 (20%)	16 (13%)	
No cockroach	255 (71%)	90 (75%)	
Missing cockroach	31 (9%)	14 (12%)	

*For differences between nonmissing multigroup comparisons using ANOVA and χ^2 distribution.
†Current NLEs other than IPT.
‡Detectable levels for dust mites (Der f 1 and Der p 1, >0.02 μg/g).
§Detectable levels for cockroach allergens (Bla g 1, >0.40 U/g; Bla g 2, >1.0 U/g).

Wellbeing Study (n = 2117) demonstrated an association between maternal report of chronic domestic violence and an increased risk of physician-diagnosed asthma in children by age 3 years, with effects attenuated when mothers maintained positive caregiving in the context of violence.[44]

These data suggest a nonlinear or threshold effect in that among women who had experienced IPT, the prevalence of more extreme increased levels of IgE in their infants at birth increased. Also, sensitivity analysis demonstrated that results were strongest when considering more extreme cutoff values for increased cord blood IgE (≥1.08 and ≥1.40 IU/mL). The more extreme levels might be most relevant as a preclinical marker of atopic disorders that develop in later childhood. Although there is no agreement on the threshold level that is associated with increased risk of clinical atopic disorders, several studies have found that cord blood IgE levels between 0.9 and 1.3 IU/mL are associated with significantly increased risk, particularly in relation to early sensitization in later childhood.[38,45] Indeed, cord blood IgE levels in general are a weaker predictor of later atopic risk unless the more extreme levels are considered. Use of lower cutoff values in prior research[46] results in significant changes in the sensitivity, specificity, and positive predictive value. Moreover, although population studies suggest that most children with atopic disease do not have increased IgE levels as newborns, those with especially increased IgE responsiveness are particularly predisposed to allergic disorders.

Strengths and limitations

The strengths of the current study include the assessment of trauma in different life periods using identical items, adjustment for a range of confounders across the life course and potential mediators, and the focus on a population at high risk for both trauma and atopy. Nevertheless, limitations should be noted.

First, all participants were recruited from specific prenatal clinics or affiliated WIC sites. These mothers might differ systematically from those not receiving prenatal care at these centers or participating in WIC, limiting generalizability.

Second, because measures of IPT are self-reported and retrospective, the potential for recall bias or social desirability response bias remains. However, any reporting bias would likely be in the direction of underreporting, biasing our results toward the null. Furthermore, the R-CTS is generally reliable because it asks about discrete objective events rather than global estimates of family interaction, which are less prone to inaccurate recall.[47,48] Subjects might also inaccurately recall when past events have occurred. Although a blurring together of repeated events over childhood is possible, this is less likely to occur when subjects are asked to report for an age range (≤11 years or 12-17 years of age) rather than a specific age for each event.[47]

Third, although our sensitivity analyses suggest a threshold relationship between maternal lifetime IPT and cord blood IgE levels, we acknowledge that a dose-response relationship could be more rigorously explored by using a continuous measure of IPT. Although the R-CTS ascertains information on discrete types of violence, it does not capture other salient contextual features indicating violence severity (family/relationship context [ie, relationship of the perpetrator to the victim], injury severity, and abuse frequency). The lack of such salient information might have reduced the predictive power of the maternal IPT variables.

Finally, these analyses did not include psychologic or physiologic correlates of chronic prenatal stress, which future work should examine to test more directly the posited underlying mechanisms.

These analyses provide the first suggestion that maternal experiences of IPT might have transgenerational implications for asthma and allergy risk. The findings underscore the need to consider maternal stress beyond that experienced only during pregnancy when exploring intergenerational effects. Future studies linking maternal stress to chronic atopic diseases should consider a life-course approach.[49] Further study of associations

TABLE III. Distribution of cord blood IgE and geometric mean of IgE levels by IPT exposure

	Cord blood IgE level					
		Percentiles				
Periods of IPT	% Nondetectable (LLOD <0.20)	25%	50%	75%	Maximal	Geometric mean* (CI)
All	24.7	0.20	0.51	1.08	100	0.50 (0.45-0.56)
No exposure	24.2	0.20	0.46	0.91	46.3	0.46 (0.40-0.53)
Early-life IPT	23.4	0.21	0.54	1.55	14.9	0.57 (0.44-0.73)
Late-life IPT	27.6	0.14	0.51	1.65	3.6	0.49 (0.30-0.80)
Chronic IPT	28.1	0.17	0.67	1.56	100	0.61 (0.41-0.90)

LLOD, Lower limit of detection.

TABLE IV. Maternal IPT exposure and cord blood total IgE levels: Logistic regression analyses

	Cord blood (n = 478)				
		Multivariate models			
Predictors	Unadjusted models	Model 1*	Model 2†	Model 3‡	Model 4§
Periods of IPT					
No IPT	—	—	—	—	—
Childhood/ teen only	1.78¶ (1.05-3.00)	1.48 (0.85-2.58)	1.52 (0.86-2.66)	1.45 (0.82-2.55)	1.43 (0.81-2.52)
Adult/pregnancy only	2.23‖ (0.97-5.13)	2.19‖ (0.90-5.33)	2.22‖ (0.91-5.43)	2.33‖ (0.95-5.70)	2.19‖ (0.89-5.38)
Chronic IPT (both)	2.25¶ (1.19-4.24)	2.10¶ (1.07-4.15)	2.21¶ (1.09-4.49)	2.19¶ (1.08-4.46)	2.18¶ (1.06-4.50)

Results are presented as ORs and 95% CIs.

*Model 1 adjusts for maternal age, child's sex, maternal race, maternal education, current economic difficulties, season of birth, and parental home ownership.

†Model 2 adjusts for maternal age, child's sex, maternal race, maternal education, current economic difficulties, parental home ownership, season of birth, and other current NLEs.

‡Model 3 adjusts for maternal age, child's sex, maternal race, maternal education, current economic difficulties, parental home ownership, season of birth, other current NLEs, and household allergens.

§Model 4 adjusts for maternal age, child's sex, maternal race, maternal education, current economic difficulties, parental home ownership, other current NLEs, household allergens, season of birth, birth weight for gestational age, maternal atopy, and maternal smoking during pregnancy.

‖$P < .10$.

¶$P < .05$.

between maternal IPT and child atopic risk should incorporate methodologies that minimize recall bias and assess IPT severity. Because interpersonal violence disproportionately affects members of racial/ethnic minorities and those of lower SES, such exposures might in part explain the excess burden of atopic disorders in these populations and warrants further research.[9] Continued follow-up of this prospective pregnancy cohort will reveal whether lifetime maternal IPT influences the expression of allergic sensitization and asthma expression in these children.

Clinical implications: Studies examining prenatal stress and childhood atopy risk should also consider stress before pregnancy by taking a life-course perspective. Maternal chronic life stress, particularly IPT, might influence the child's developing immune system.

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