Prenatal and Postnatal Maternal Stress and Wheeze in Urban Children

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increased prenatal maternal nervousness predicted elevated cord blood IgE adjusting for family history, maternal age, education, and prenatal smoking (14). An Australian study (n = 5,810) linked higher prenatal anxiety to increased asthma with airway hyperesponsiveness in school-aged children adjusting for sex, prematurity, maternal age, education, atopy, prenatal smoking, and postnatal maternal anxiety (15). Reyes and colleagues

considered only prenatal BC. Multivariate logistic regression analyses first considered associations between the NLEs score and child wheeze including prenatal and postnatal NLEs in separate models (i.e., independent effects of stress in each respective period). The NLEs score was categorized *a priori* as 0, 1–2, 3–4, or greater than or equal to 5 to assess exposure-response relationships and the possibility of nonlinearity. To examine the effects of the combination of prenatal and postnatal NLEs, we next collapsed NLEs scores into low (0–2, at or below the median) and high (⩾3, above the median) groups, and categorized maternal stress into four combinations: (*1*) low prenatal–low postnatal, (*2*) high prenatal–low postnatal, (*3*) low prenatal–high postnatal, and (*4*) high prenatal–high postnatal stress. This model examined whether stress in one developmental period (prenatal or postnatal) or stress persisting over both sensitive developmental periods was most significantly associated with child repeated wheeze, compared with low stress in both periods. To ensure these results were not unduly affected by the choice of NLE cutpoints, we also explored the exposure-response relationships considering NLEs as continuous z9(NLE–(T)mneral0.1(i)1z.3(n)4)4.1(65)-349ddit5.31(i)1e9(NL7-459.(con)-8(mo5(a)11.ild)]TJT0.012T(GAMsdian)-78w

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								ч, Bla g 1		ч, Bla g 2	
		r	P	R	P	r	P	r	P	r	P
		0.[illegible]	<0.001								
		0.20	<0.001	0.21	<0.001						
ч,	Bla g 1	0.0	0.10	0.0	0.21	0.1	<0.001				
ч,	Bla g 2	0.03	0.4	0.0[illegible]	0.2	0.1[illegible]	<0.001	0. 0	<0.001		
, z		0.13	<0.001	0.1	<0.001	0.[illegible]	<0.001	0.20	<0.001	0.1	<0.001

Definition of abbreviations = Bla g = Blatella germanica = .

Mothers were primarily ethnic minority (55% Hispanic, 29% African American), low socioeconomic status (62% having ⩽12 yr of education), and nonsmokers during pregnancy (80%); 80 (12%) children had repeated wheeze. The prevalence of stress experienced across the stress domains based on wheeze status is shown in Table E2.

Table 3 presents the exposure-response relationship across NLEs categories in relation to wheeze, considering prenatal and postnatal NLEs in separate models. In models adjusted for child sex and season of birth (Model 1), children born to mothers in the highest-exposure group compared with those born to women with lowest stress had approximately threefold to fourfold increased odds of repeated wheeze, with similar effects for prenatal and postnatal stress. Effects remained significant in fully adjusted models (Model 3). Further inclusion of maternal BMI, smoking, and birthweight did not substantively alter these findings (data not shown). Penalized spline regressions confirmed a linear exposure-response relationship (Figure 1).

Figure 2 presents the results from fully adjusted models comparing those reporting high–high, low–high, and high–low prenatal–postnatal stress combinations with those reporting low stress in both periods. Children born to mothers with high stress in both pregnancy and the postpartum period were significantly more likely to have repeated wheeze (adjusted odds ratio [OR], 3.04; 95% confidence interval [CI], 1.67–5.53) compared with children of mothers reporting low stress in both periods. This finding was further confirmed by fitting bivariate penalized splines showing the joint effects of prenatal and postnatal NLEs as continuous indicators (*see* Figure E1).

The multivariable logistic regression models also showed that boys were more likely to have repeated wheeze compared with girls (adjusted OR, 2.28; 95% CI, 1.34–3.88) and maternal atopy was associated with increased repeated wheeze (adjusted OR, 1.58; 95% CI, 0.95–2.64), although the latter was borderline insignificant.

Figure 3 shows the relationship between prenatal NLEs and repeated wheeze stratified by maternal sensitization indexed by any specific IgE level greater than or equal to 0.35 kU/L measured during pregnancy. We observed a significant positive association between the higher NLEs score (⩾3) relative to lower stress (NLEs 0–2) and repeated wheeze in children born to mothers without a positive specific IgE level (adjusted OR, 2.35; 95% CI, 1.04–5.29) but not in the sensitized group (adjusted OR, 0.27; 95% CI, 0.07–1.08) (P for interaction = 0.03).

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(range 0–9)		(%)	[illegible]%	[illegible]%	[illegible]%	[illegible]%
			Prenatal NLEs Model			
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This study adds to the literature in three important ways. To our knowledge, these are the first prospective human data to show an exposure-response relationship between greater prenatal and postnatal maternal stress, when considered independently, and increased odds of early childhood repeated wheeze. Moreover, although children had heightened sensitivity to maternal stress *in utero* and in early childhood, those with higher maternal stress in both developmental periods were most likely to have recurrent wheeze. Also, effects of prenatal stress were modified based on whether mothers were sensitized to aeroallergens. Notably, observed effects remained significant when adjusting for a number of important confounders and pathway variables.

Our data indicate that cumulative exposure to greater maternal stress in the prenatal and early postnatal period was more significantly associated with repeated wheeze rather than suggesting the import of one developmental period over the other. This is consistent with other evidence suggesting that prenatal stress and psychologic correlates in mothers act in concert with postnatal stress-related factors (e.g., disrupted caregiver–child interactions) to further shape or program offspring regulatory systems that may contribute to wheeze expression (9, 30). Prenatal stress may disrupt maternal physiology (e.g., HPA axis, sympathetic-adrenal-medullary system, immunomodulation), which then may potentiate the developing fetal immune system (e.g., up-regulating maternal and fetoplacental Th2 cytokine or natal shu2278sso05-1.48shs259).4553.4mayne454l8s)g(nh2.5(ifl0(u2278se)g(nh2-304c)05-42.04c)05o)19(m)05m22715osoh2.5(il)05o

in urban children. These findings may have implications for designing prenatal and postnatal psychosocial or stress-reduction interventions to reduce respiratory disease in children. For example, interventions at the individual level may be more effective if initiated during pregnancy and then extended through early child development. On a broader scale, policy-level interventions that improve socioeconomic circumstances with consequent decreased exposure to stress across a multitude of life domains in pregnant women and young families also have potential to reduce adverse respiratory outcomes in early life.

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