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Secure Base Representations in Children With Asthma: Links With Symptoms, Family Asthma Management, and Cytokine Regulation

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Children's perceptions of caregivers as a secure base have been linked with socioemotional outcomes, but little is known about connections to physical health. We examined whether secure base representations are associated with children's symptoms, family management strategies, and inflammatory processes in children with asthma. Participants included 308 children (ages 8–17) and one parent. Children completed a blood draw to measure asthma-related immune functions and reported on perceptions of their mothers as a secure base and their asthma symptoms. Dyads completed interviews about asthma management. Analyses revealed that children's secure base perceptions were associated with better family asthma management and lower Type 2 T-helper cell cytokine production. These findings suggest that secure base representations may be protective for children with asthma.

The availability of a responsive and dependable caregiver is critical to healthy development across the life span (Bowlby, 1969/1982, 1973). Bowlby (1982) proposed that children develop experience-based mental representations of their caregivers' availability and responsiveness during times of need. These representations, or "internal working models," develop in the first year of life and reflect the extent to which the child perceives the parent as a "secure base" from which to explore and as a "safe haven" to which to return in times of threat or distress (Bowlby, 1988). Over time, children develop regulatory strategies for managing their own emotions but continue to seek comfort from attachment figures when distressed. Access to a secure base enables children to explore the world and seek help or comfort when confronted with threat (Bowlby, 1973). Further, within close relationships, secure individuals are able to engage in open, flexible expression of emotions (Kobak & Duemmler, 1994; Oppenheim, Koren-Karie, & Sagi-Schwartz, 2007), thus allowing for negative feelings to be expressed and mitigated. In contrast, individuals lacking confidence in a secure base have not had the experience of being able to rely on a consistent caregiver to meet their emotional needs. As a result, these individuals struggle to manage their negative emotions and have difficulty communicating their needs within the context of close relationships (Cassidy & Kobak, 1988; Kobak, Cole, Ferenz-Gillies, Fleming, & Gamble, 1993).

To date, the majority of research on outcomes associated with children's attachment experiences has focused on how attachment is linked with children's social and emotional functioning (e.g., Groh, Fearon, van IJzendoorn, Bakermans-Kranenburg, & Roisman, 2017). In the last several decades, however, attachment research has expanded beyond studies of socioemotional outcomes to include studies on attachment-related links to neurobiological development (e.g., Schore, 2001), physiological stress reactivity (e.g., Nachmias, Gunnar, Mangelsdorf, Parritz, & Buss, 1996), and autonomic nervous system activity (e.g., Diamond & Hicks, 2005). Recently, there has been interest in examining

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potential links between indicators of attachment security and measures of physical health (e.g., Jones et al., 2017; Puig, Englund, Simpson, & Collins, 2013; see also Ehrlich, Miller, Jones, & Cassidy, 2016; Pietromonaco, Uchino, & Dunkel Schetter, 2013, for reviews). One example comes from the Minnesota Longitudinal Study of Parents and Children, a study that has followed children for over 30 years (Puig et al., 2013). In this sample, individuals who were securely attached in infancy reported fewer inflammation-based illnesses compared with adults who were classified as insecurely attached in infancy. Additional evidence comes from Jones et al. (2017), who examined the prospective association between adolescents' perceptions of parents as a secure base and C-reactive protein (CRP)—an indicator of low-grade chronic inflammation—in adulthood. Adolescent perceptions of having a parent they could depend on in adolescence were associated with lower levels of CRP 20 years later, even after controlling for possible inflammation-related confounds, including cigarette use and body mass index.

These studies of attachment have examined health-related outcomes in early and middle adulthood—a phase of life when research can measure biomarkers (e.g., high blood pressure, low-grade inflammation) that reliably forecast later health problems (e.g., diabetes, heart attacks, strokes). But studies linking attachment and health in childhood and adolescence are often difficult to conduct because few youth have overt disease, and the validity of biomarkers is less well established. One way to circumvent this constraint is to study a sample of children who have a chronic disease, such as asthma and Type 1 diabetes. There are two key advantages to this disease-centered approach: First, it allows researchers to examine whether children's attachment is associated with clinically relevant outcomes, such as illness symptoms and functional limitations; and second, it permits a focus on biological processes that are known to contribute to the disease's underlying pathophysiology (Miller, Chen, & Cole, 2009). Both of these features enhance the clinical relevance of this research.

Asthma is a particularly suitable disease to study in this context because it is the most common chronic disease in childhood, affecting over 7 million children in the United States (Bloom, Jones, & Freeman, 2013). Asthma is a respiratory disease that includes inflammation and obstruction of the airways (Busse & Lemanske, 2001). Cells of the immune system play a key role in these processes: Following exposure to allergens, pollutants, infections, and other stimuli, these cells launch an inflammatory response in the airways that results in mucus production, airway constriction, and difficulties breathing. T-helper lymphocytes are a key cellular player in the airway inflammatory response, which they coordinate through signaling molecules known as cytokines. Broadly speaking, these molecules can be grouped into Type 1 T-helper cell (Th1) cytokines (e.g., interferon [IFN]-γ, interleukin [IL]-2), which mobilize responses against intracellular pathogens, and Type 2 T-helper cell (Th2) cytokines (e.g., IL-4, IL-5, IL-10, IL-13), which mobilize responses against extra-cellular pathogens. Both kinds of responses are dysregulated in asthma, although Th2 cytokines are thought to be especially involved in recruiting cells to the airways, and activating them in ways that promote excessive mucus production and airway constriction.

A growing body of literature has identified various psychosocial factors, including family experiences, that are associated with asthma symptoms (e.g., Chen & Schreier, 2008; Kaugars, Klinnert, & Bender, 2004; Shalowitz, Berry, Quinn, & Wolf, 2001). Only two studies have explored connections between children's attachment and asthma, however. Both Mrazek, Casey, and Anderson (1987) and Cassibba, van IJzendoorn, Bruno, and Coppola (2004) found that children with asthma were more likely to be insecurely attached compared with children without asthma. These studies highlight the possibility that asthma symptoms (e.g., difficulties with breathing, chest tightness) can be frightening for children and parents alike, and these worries might encourage parents to be overprotective and anxious; such parenting behaviors, in turn, might inhibit children's exploration of the environment and foster insecure-ambivalent attachments for children. These studies were designed to consider attachment differences between healthy children and children with asthma, so it is unclear how attachment representations *within* a sample of children with asthma might predict variations in children's asthma symptoms.

We propose that children who perceive their parent as a secure base have confidence in their caregiver's ability to help them manage a complicated, multifactorial illness like asthma. Such confidence likely reflects parents' superior strategies in managing children's asthma (e.g., preventing exposure to triggers, closely monitoring symptoms, adhering to medication routines, and taking appropriate actions when asthma flare-ups arise). Given these management strategies, children may experience fewer

symptoms and have fewer limitations as a result of their asthma. These patterns may emerge because children who have a secure base have confidence that their symptom distress will be attended to and resolved rather than minimized or exaggerated.

We also suggest that individual differences in children's ability to use their parent as a secure base may correspond to differences in inflammatory processes thought to underlie asthma. Previous studies have identified links between family experiences and children's asthma-related inflammatory processes (e.g., Chen et al., 2006; Ehrlich, Miller, & Chen, 2015; Schreier & Chen, 2010; Tobin et al., 2015). For example, chronic family stress has been associated with higher *in vitro* production of the Th2 cytokines IL-5 and IL-13 (Chen et al., 2006), and family routines have been shown to be protective against these apparently excessive responses (Schreier & Chen, 2010). Similarly, Tobin et al. (2015) found that observations of maternal responsiveness (measured via naturalistic observations using the Electronically Activated Recorder) were negatively associated with IL-5 and IL-13. Confidence in the availability of a caregiver may promote a variety of health benefits for children with asthma. As described earlier, children who have confidence in receiving support from a caregiver may use better behavioral strategies (e.g., monitoring symptoms, using medication appropriately, asking for help), all of which could help prevent exacerbations in inflammatory processes that lead to worsening asthma symptoms.

In the present study, we addressed three research aims. Our first aim was to investigate the association between children's perceptions of their mothers as a secure base and their asthma symptoms. We hypothesized that perceptions of mothers as a secure base would be negatively associated with children's asthma symptoms. Second, we examined the connections between secure base representations and family asthma management behaviors. We utilized interviewer ratings of eight domains of family asthma management. We hypothesized that secure base use would be associated with some, but not all, aspects of family management of asthma. For example, children who perceive their parents as a secure base should take more proactive and appropriate steps to monitor and treat their asthma symptoms, which could include seeking help from their parents to control their symptoms. In contrast, we did not expect secure base representations to be associated with ratings of exposure to environmental triggers—a measure that reflects the family's attempts to minimize dust and allergens in the home. (In other words, we did not expect the cleanliness of the home to vary as a function of children's secure base representations.) Finally, our third aim was to explore the associations between children's perceptions of their mothers as a secure base and children's asthma-relevant inflammatory processes by examining how aggressively children's cells respond with Th-2 and Th-1 cytokines when exposed to mitogens in vitro.

Method

Participants

Participants included 308 children ages 8–17 who were physician-diagnosed with asthma (M_{age} = 13.0, SD_{age} = 2.5; 54.7% male). Families were recruited through one health care system (NorthShore University HealthSystem) and one federally qualified health center (Erie Family Health Center) in the greater Chicago area. Children came to the laboratory with one parent (88.0% mothers, 11.7% fathers) and completed the measures described in the following section. Families were required to be fluent in English, and children had to be free of acute respiratory illness at the time of the visit and have no other chronic physical illnesses other than asthma. Among children, 60.4% were White, 25.6% were Black/African American, 12.0% were Asian, and 16.6% were Hispanic. (Participants were allowed to select more than one ethnic/racial category.) Most parents (75.0%) were married and living with their spouse, with remaining parents reporting that they were single (12.3%) or separated/divorced (11.0%). There was considerable variability in the socioeconomic status of families in this study. Although the median household income was $100,000, approximately a quarter of the families (24.1%) received government assistance (primarily Medicaid and Supplemental Nutrition Assistance Program benefits). Most parents (84.4%) reported some college education.

This study was approved by the Northwestern University, NorthShore, and Erie Institutional Review Boards. Data were collected between July 2013 and June 2016. Parents and children each received $80 for participating in the study visit.

Measures

Children's Perceptions of Mothers as a Secure Base

Children completed the 13-item Parent as a Secure Base Scale-Revised (Cassidy & Woodhouse,

2003; Woodhouse, Dykas, & Cassidy, 2009). Children completed the measure about their perceptions of their mothers as an available, responsive, and sensitive secure base ($\alpha = .90$) using a 1–5 scale, with higher ratings indicating greater secure base provision. Sample items include "My mother is someone I can count on when I need help" and "my mother is there for me in times of trouble." Previous use with this scale has shown that scores correlate with adolescent perceptions of parental warmth and understanding (Cassidy, Ziv, Rodenberg, & Woodhouse, 2003; Dykas, Ziv, Woodhouse, & Cassidy, 2007) as well as mothers' and fathers' self-reported depressive symptoms (Woodhouse, Ramos-Marcuse, Ehrlich, Warner, & Cassidy, 2010).

Self-Reported Asthma Symptoms

Children completed the Asthma Control Test (ACT), which is a five-item questionnaire that assesses asthma symptoms, use of rescue medications, and the effects of asthma on children's daily functioning over the past 4 weeks (Nathan et al., 2004; Schatz et al., 2006). Scores on this measure can range from 5 to 25, with higher scores indicating well-controlled asthma ($\alpha = .84$). Children also completed the Pediatric Asthma Quality of Life Questionnaire (AQL; Juniper et al., 1996), a 23-item measure with three subscales that tap children's asthma symptoms, activity limitations, and emotional functioning (αs ranging from .85 to .94). The asthma symptoms subscale includes 10 items that assess frequency of cough, wheezing, and waking at night due to asthma symptoms. The activity limitations subscale includes five items that tap limitations in sports and daily activities. Finally, the emotional functioning subscale assesses children's negative emotions related to asthma symptoms (e.g., fear, frustration, irritability). Higher scores on these subscales indicate fewer symptoms and limitations.

Family Asthma Management

Parents and children were interviewed together about asthma management knowledge, beliefs, and behaviors in the past 6 months using the semistructured Family Asthma Management System Scale (McQuaid, Walders, Kopel, Fritz, & Klinnert, 2005). Families were subsequently rated by interviewers on eight domains using a 1–9 scale, with higher ratings indicating better asthma management. Five percent of interviews were coded by 6–8 coders, and reliability was assessed throughout the study period. Intraclass correlation coefficients ranged from .71 to .98. The eight scales capture a comprehensive picture of the family's knowledge about asthma, and their attempts to manage children's symptoms, minimize exposure to triggers, and balance asthma management with demands of daily life. For each of the scales below, higher scores indicate better knowledge or family management.

Specifically, the *asthma knowledge* scale reflects families' understanding about the biology of asthma and how medications function to treat asthma symptoms. For the *knowledge and assessment of symptoms* scale, interviewers probe for details about the extent to which families are able to describe the course of children's symptoms, triggers, seasonal patterns, and early warning signs. The *child's response to symptoms and exacerbations* scale assesses children's plans for monitoring and managing symptoms, particularly when away from immediate family members. The *family's response to symptoms and exacerbations* scale measures how the family collectively responds to children's asthma symptoms (e.g., monitoring symptoms, using medication, seeking additional help if symptoms do not subside). Interviewers assess strategies that families use to reduce children's exposure to asthma triggers using the *environmental control* scale, which includes questions about smoke exposure and additional preventive strategies to limit exposure (e.g., air filters, washing sheets frequently). Ratings also reflect whether there are pets that have free access throughout the home (including bedrooms). Parents and children answer questions about compliance with children's asthma medication, whether children have access to rescue medications at all times, and any strategies they use to remember to take medications, all of which contribute to scores on the *adherence with asthma medications* scale. In addition, as part of the *collaborative relationship with provider* scale, parents and children report about their frequency of visiting their doctor, their comfort with asking questions, and whether they have had any discussions with their provider about a treatment plan for asthma. Finally, interviewers rate the family on their *balanced integration of asthma into family life*. Ratings for this scale are based on the family's descriptions of the extent to which asthma limits activities, interferes with routines, and creates complications in their life.

Cytokine Production

We measured stimulated cytokine secretion by peripheral blood mononuclear cells (PBMCs).

Antecubital blood was drawn into BD Cell Preparation Tubes (Becton Dickinson, Franklin Lakes, NJ) containing sodium heparin. PBMCs were then isolated by density-gradient centrifugation according to manufacturer instructions and dispensed into the wells of culture plates containing a common mitogen known to generate Th1 and Th2 cytokine release. We incubated 0.5×10^6 PBMCs with 25 ng/ml of phorbol 12-myristate 13-acetate (PMA; Sigma-Aldrich, St. Louis, MO) + 1 μg/ml of ionomycin (INO; Sigma-Aldrich) for 24 hr at 37°C in 5% CO_2 (see Chen et al., 2017). We included an unstimulated well on the same plate with the same number of PBMCs with no mitogen. At the end of the incubation, supernatants were harvested by centrifugation and frozen at −80°C until assayed in batch via electrochemiluminescence on a SECTOR Imager 2400A (Meso Scale Discovery [MSD], Rockville, MD). This instrument gives accurate, sensitive multiplex readouts across a wide range (Chowdhury, Williams, & Johnson, 2009). We used MSD's Human Th1/Th2 7-Plex Tissue Culture Kit, which measures both Th2 (IL-4, IL-5, IL-10, and IL-13) and Th1 (IFN-γ, IL-2) cytokines. Mean intra-assay coefficients of variation ranged from 1.97% to 4.14%. Cytokine responses were quantified by subtracting values in the unstimulated well from those in the PMA/INO well.

Potential Covariates

Variables used as covariates in statistical analyses included asthma severity, determined from the National Asthma Education and Prevention Program/Expert Panel Report 2 guidelines based on the higher of symptom frequency and medication use (Bacharier et al., 2004). Children also brought in their asthma medications to the laboratory, and researchers probed families for information regarding the number of days (0–7) children used inhaled corticosteroid and beta-agonist medications in the past week. Children self-reported their depressive symptoms using the 13-item anxious/depressed scale from the Youth Self-Report (Achenbach & Rescorla, 2001; $\alpha = .84$). Children reported on the frequency of parental hostility using a 14-item scale developed by Brody et al. (2001). Higher scores indicate less parental hostility. In addition, we included demographic characteristics in all analyses, which include age, ethnicity (White/non-White), gender, and parental education (measured as total years of education).

Results

Preliminary Analyses

Intercorrelations of principal variables are presented in Table 1. Because of significant skew on the parent as a secure base scale, we performed a log transformation prior to running analyses. In addition, four participants with extreme values (± 3 *SD* from the mean) for the cytokine stimulation data were removed prior to analysis.

Data Reduction

In order to reduce the number of outcome variables, we conducted three series of principal components analyses (PCAs). First, we subjected children's reports on the ACT and AQL symptom scales to a PCA with varimax rotation. All scales loaded onto a single *Asthma Symptoms* factor, which accounted for 78.5% of the variance (all loadings > .83). Higher scores on this factor reflect fewer symptoms and limitations.

Second, we reduced the asthma management outcomes with the same PCA approach. The first component, which explained 44.7% of the variance, reflected *Asthma Knowledge* and included interviewer ratings on the asthma knowledge, knowledge of symptoms, child's response to symptoms, and family's response to symptoms (all loadings > .64). The second component, which explained 16.0% of the variance, included ratings for children's adherence with asthma medications, collaborative relationship with provider, and balanced integration of asthma (all loadings > .74), so we labeled this component *Living With Asthma*. The environmental control rating did not load well onto either factor and was kept separate. As with the self-reported composite score calculation noted earlier, for each composite score, we first standardized individual scales on each factor and then calculated a mean factor score.

Finally, we conducted PCAs to aggregate cytokine responses to PMA/INO stimulation (see Chen et al., 2017). Prior to the running the PCAs, we first log-transformed all cytokine variables that had skewness values of 2.0 or greater. In each PCA, cytokines loaded onto Th2 (IL-4, IL-5, IL-10, and IL-13) and Th1 (IFN-γ, IL-2) factors, as expected. The Th2 factor accounted for 68.1% of the variance, and cytokine loadings ranged from .87 to .97. The PMA/INO Th1 factor accounted for 19.4% of the variance and had cytokine factor loadings of .73 and .97. Based on this PCA, we created separate Th1 and Th2 cytokine factors by first standardizing each cytokine value

Table 1
Correlations Among Principal Variables in the Present Study

Variable	1	2	3	4	5	6	7
1. Child secure base perceptions	—						
2. Child-reported asthma symptoms	.12*	—					
3. FAMSS asthma knowledge	.13*	.00	—				
4. FAMSS living with asthma	.22***	.21***	.48***	—			
5. FAMSS environmental control	.00	.08	.00	.14*	—		
6. PMA/INO Th1 cytokines	−.07	−.10	−.10	−.11	.00	—	
7. PMA/INO Th2 cytokines	−.17**	.05	−.06	−.14*	.10	.33***	—

Note. Higher factor scores indicate better knowledge, management, or environmental control. FAMSS = Family Asthma Management System Scale; PMA = phorbol 12-myristate 13-acetate; INO = ionomycin; Th1 = Type 1 T-helper cell; Th2 = Type 2 T-helper cell.
*$p < .05$. **$p < .01$. ***$p < .001$.

(original or log-transformed, as appropriate) and then averaging the standardized scores.

Perceptions of Mothers as a Secure Base and Child Report of Symptoms

Our initial analysis examined whether children's perceptions of their mothers as a secure base were associated with child reports of symptoms and daily functioning in relation to asthma. As shown in Table 2, children's perceptions of their mothers as a secure base were associated with fewer asthma symptoms. In Step 2, we included children's depressive symptoms and child-reported parental hostility as additional predictors; children's depressive symptoms and child-reported hostility were associated with children's self-reported asthma symptoms.

Table 2
Perceptions of Mothers as a Secure Base and Child Report of Symptoms

Predictors	β	*p*
Step 1		
Child age	.16	.004
Child race	−.10	.07
Child gender	.19	< .001
Parent education	.11	.04
Child inhaled corticosteroid use	.04	.44
Child beta antagonist use	−.29	< .001
Child secure base perceptions	.14	.008
Step 2		
Child age	.16	.002
Child race	−.11	.04
Child gender	.12	.02
Parent education	.11	.03
Child inhaled corticosteroid use	.03	.53
Child beta antagonist use	−.28	< .001
Child depressive symptoms	−.32	< .001
Child-reported parental hostility	.15	.01
Child secure base perceptions	−.08	.23

Note. Higher scores on the outcome measure indicate fewer symptoms and better functioning. Race coded as 1 = White, 2 = non-White. Gender coded as 0 = female, 1 = male.

Perceptions of Mothers as a Secure Base and Family Asthma Management

Next, we examined the relation between perceptions of mothers as a secure base and the composite asthma management factors (described earlier). As shown in Table 3, perceptions of mothers as a secure base were marginally associated with the Asthma Knowledge factor and were significantly associated with the Living With Asthma factor. In contrast, secure base provision was not associated with environmental control. Children's depressive symptoms and child-reported parental hostility were not associated with the asthma management factors, however.

Perceptions of Mothers as a Secure Base and Cytokine Production

Finally, our last analysis examined the relation between children's perceptions of their mothers as a secure base and cytokine production following exposure to PMA/INO (Table 4). Analyses revealed that perceptions of mothers as a secure base were associated with lower Th2 cytokine responses to PMA/INO but not Th1 cytokine responses. Children's depressive symptoms and child-reported parental hostility were not associated with Th2 or Th1 cytokine responses.

Discussion

The present study is the first to demonstrate that individual differences in children's perceptions of

Table 3
Perceptions of Mothers as a Secure Base and FAMSS Factor Scores

	Asthma Knowledge		Living With Asthma		Environmental control	
Predictors	β	*p*	β	*p*	β	*p*
Step 1						
Child age	.02	.41	−.07	.19	−.16	.006
Child race	.00	.99	−.12	.02	.13	.04
Child gender	−.07	.20	.06	.22	.07	.20
Parent education	.20	.001	.19	< .001	.14	.02
Child inhaled corticosteroid use	.13	.03	.37	< .001	.07	.27
Child beta antagonist use	.08	.17	.00	.99	−.05	.40
Child asthma severity	.02	.80	−.14	.008	−.09	.12
Child secure base perceptions	.10	.07	.14	.008	−.03	.59
Step 2						
Child age	.03	.62	−.07	.20	−.17	.005
Child race	.01	.83	−.12	.03	.12	.05
Child gender	−.04	.48	.07	.18	.06	.31
Parent education	.20	.001	.19	< .001	.14	.02
Child inhaled corticosteroid use	.13	.03	.37	< .001	.07	.25
Child beta antagonist use	.09	.15	.00	.98	−.05	.39
Child asthma severity	.01	.83	−.15	.008	−.10	.12
Child depressive symptoms	.11	.09	.03	.57	−.04	.51
Child-reported parental hostility	.05	.44	.01	.87	−.06	.41
Child secure base perceptions	.12	.09	.15	.02	−.02	.81

Note. Higher factor scores indicate better knowledge, management, or environmental control. Race coded as 1 = White, 2 = non-White. Gender coded as 0 = female, 1 = male. FAMSS = Family Asthma Management System Scale.

Table 4
Perceptions of Mothers as a Secure Base and Stimulated Cytokine Responses

	PMA/INO Th1 cytokines		PMA/INO Th2 cytokines	
Predictors	β	*p*	β	*p*
Step 1				
Child age	−.17	.009	.08	.20
Child race	.17	.007	.16	.01
Child gender	.00	.96	.02	.74
Parent education	.007	.92	.03	.66
Child inhaled corticosteroid use	−.04	.51	−.13	.04
Child beta antagonist use	.08	.22	−.07	.28
Child asthma severity	−.08	.24	−.002	.98
Child secure base perceptions	−.09	.15	−.12	.05
Step 2				
Child age	−.17	.008	.07	.24
Child race	.17	.009	.15	.02
Child gender	.01	.93	−.01	.86
Parent education	.006	.93	.03	.64
Child inhaled corticosteroid use	−.04	.56	−.13	.04
Child beta antagonist use	.08	.24	−.07	.29
Child asthma severity	−.08	.22	.01	.90
Child depressive symptoms	.02	.79	−.11	.11
Child-reported parental hostility	−.06	.41	−.01	.85
Child secure base perceptions	−.05	.54	−.16	.03

Note. Race coded as 1 = White, 2 = non-White. Gender coded as 0 = female, 1 = male. PMA = phorbol 12-myristate 13-acetate; INO = ionomycin; Th1 = Type 1 T-helper cell; Th2 = Type 2 T-helper cell.

their mothers as a secure base are associated with interviewer ratings of families' management of children's asthma and children's Th2 cytokine production. These findings are in line with a growing body of research showing that family experiences are linked with children's asthma symptoms and lung function (e.g., Chen, Bloomberg, Fisher, & Strunk, 2003), and cytokine production (Tobin et al., 2015) and fit within the broader framework of attachment theory, suggesting that children's abilities to depend on their caregivers may influence not only their socioemotional well-being but also their physical health (Ehrlich et al., 2016; Jones et al., 2017; Puig et al., 2013).

We found that children who had greater perceptions of their mothers as a secure base reported fewer self-reported asthma symptoms and limitations, although these effects were no longer significant after adjusting for children's depressive symptoms and reports of parental hostility. Clinicians and researchers often rely on children's reports of their asthma symptoms over other informant reports (e.g., parents) because other reporters often observe only a portion of children's asthma-related experiences, which can vary substantially across contexts. One question that arises from the pattern of findings reported in this study is whether children who perceive their mothers as a secure base actually exhibit fewer asthma symptoms or if they are simply less distressed by symptoms that might be more worrisome for children who lack a secure base—in other words, do children with a secure base *underreport* their symptoms? Given the

corresponding findings with secure base representations and interviewer ratings of family asthma management and biological measures of asthma-relevant inflammatory processes, it is unlikely that the observed effects are entirely the result of reporting biases. Nevertheless, this question about attachment-related reporting biases of asthma symptoms should be considered in future research.

In addition, we found that children's perceptions of their mothers as a secure base were associated with several aspects of interviewer ratings of family management of children's asthma. Specifically, children's secure base perceptions were marginally associated with composite scores reflecting asthma knowledge and were significantly associated with scores that reflect how well they are doing living with asthma. These findings are notable because the interviewer ratings for these composite scores reflect the family's responses to children's symptoms, their medication adherence, and their integration of asthma into daily life—all behaviors one would expect from a sensitive parent. In other words, these parents monitor their child's symptoms proactively instead of reactively, help their child keep a strict medication schedule to minimize exacerbations, and recognize that the child has a multifaceted life and needs to balance asthma management with other demands (e.g., sports, activities with friends). These proactive strategies to manage children's asthma may partially account for the findings (described earlier) that secure base representations were negatively associated with children's asthma symptoms.

In contrast, we found no association between children's perception of their mothers as a secure base and environmental control. On one hand, given the finding that secure base perceptions were associated with better knowledge about asthma, one might have expected that parents would also be similarly attuned to efforts to minimize environmental exposures that could exacerbate children's asthma symptoms. On the other hand, parents may have an awareness about environmental exposures but might have difficulty successfully *executing* some of the preventive strategies that lead to high scores on this scale. For instance, families will receive high scores on the environmental control scale if they remove carpeting (which traps allergens) and invest in air filters, special bedding, and thorough deep cleaning. But these strategies, although often effective at reducing children's symptoms, can be expensive, time intensive, and even impossible (e.g., renters may not be allowed to remove carpets from the home). Thus, although we expect that parents whose children view them as a secure base would have good intentions for minimizing environmental exposures, we would not necessarily expect them to have the ability to be more effective than other parents at controlling the environment.

Our use of a cell stimulation paradigm to examine children's inflammatory processes is an important strength of the study that merits some discussion. By using a cell stimulation paradigm in the present study, we were able to observe cellular *function*—that is, we could examine the extent to which cells mounted an inflammatory response (by secreting cytokines) when exposed to mitogen. This stringent study design includes important controls across participants, including controlling the number of cells exposed to the mitogen and accounting for spontaneous cytokine production during the incubation period, thereby minimizing possible alternative explanations for differences in cytokine production across participants. In addition, we assessed disease-relevant cytokines by assaying both Th2 and Th1 cytokine production following exposure to mitogen. These proteins play an important role in the signaling cascade that leads to asthma symptoms (e.g., bronchoconstriction, mucus, wheezing) and thus represent a distinct approach from measures of systemic inflammation.

Our analyses suggested that representations of mothers as a secure base were associated with Th2 cytokine production but not Th1 cytokine production when cells were stimulated with PMA/INO. Although secure base perceptions significantly predicted Th2 but not Th1 cytokines, effect sizes were not substantially different across models, so we are reluctant to draw firm conclusions about specificity here; such inferences will have to await findings in other samples. Of note is that Th2 cytokines are particularly relevant in the signaling cascade identified in the pathophysiology of asthma (e.g., Barnes, 2008; Romagnani, 2000). However, we should note that other studies have found links among psychosocial factors and both Th2 and Th1 cytokines (e.g., Marin, Chen, Munch & Miller, 2009), which is consistent with the fact that Th1 cytokines, particularly IFN-γ, are upregulated to suppress the production of Th2 cytokines (Barnes, 2001). Future research should continue to explore the correlates of secure base representations and children's adaptive cytokine responses.

Notably, although children's perceptions of their mothers as a secure base were significantly correlated with their reports of parental hostility ($r = .57$) and depressive symptoms ($r = -.41$),

secure base perceptions continued to predict family asthma management and cytokine production when these variables were included as potential covariates. In contrast, once we accounted for depressive symptoms and perceived parental hostility, secure base perceptions were no longer significantly associated with self-reported symptoms. Depressive symptoms and perceived parental hostility could be important mechanisms that explain the link between secure base perceptions and asthma symptoms—a model that should be tested in future research with longitudinal studies.

Although these findings provide insight into the ways in which parent–child relationships are associated with children's asthma, several limitations will be important to address in future research. First, our cross-sectional study design prohibits any tests that can evaluate questions about causality or directionality of effects. Longitudinal studies will be important for addressing questions about the interrelations of secure base use and asthma symptoms and inflammatory processes. For example, given evidence that inflammatory processes can shape perceptions of social connectedness (Eisenberger, Inagaki, Mashal, & Irwin, 2010), it may be that proinflammatory states in children shape their attachment representations. Similarly, longitudinal studies could address questions about whether changes in children's representations of parents forecast changes in asthma outcomes. In addition, longitudinal studies will allow for examination of possible mechanisms (e.g., medication adherence, stress regulation) that can help shed light on why children's perceptions of their parent as a secure base is associated with asthma outcomes.

Second, due to time constraints, children in our study only reported about their representations of their mothers as a secure base, and we do not know how representations of fathers or other caregivers might be similarly or uniquely associated with symptoms and inflammatory processes. Further, an important question to address in future research will be to consider family systems effects—that is, to what extent can a supportive parent offset detrimental outcomes associated with an unsupportive parent in the home? Although children often demonstrate consistency in representations of their mothers and fathers as secure bases (e.g., Woodhouse et al., 2010), some children can rely on one parent but not another, and these children may be buffered by the supportive caregiving provided by the dependable parent. Indeed, children may only need one supportive caregiver, who can help monitor children's symptoms, ensure compliance with medications, and work to maintain a balanced life despite limitations due to asthma. Alternatively, a harsh and unsupportive parent in the home, independent of a supportive caregiver, might create chaos and instability, thus fostering a family emotional climate that disrupts children's abilities to manage their asthma effectively. These possibilities should be considered in future research.

We also note that across analyses, our observed effect sizes were small, so it is likely that additional factors, both social and biological, may explain variation in asthma symptoms, management, and underlying inflammatory processes. Researchers who are exploring the correlates of asthma functioning in children should consider additional protective factors, such as facets of children's temperament or environmental and contextual factors (e.g., neighborhood pollution, strong community support). These efforts will help inform the development of interventions and prevention programs for children with asthma.

In summary, our study highlights the significance of representations of mothers as a secure base for children with asthma. Decades of research have shed light on the links between attachment and children's social and emotional development, and our findings suggest that attachment representations may also play an important role in health outcomes as well, including children's asthma symptoms, management of asthma, and inflammatory processes.

References

Achenbach, T. M., & Rescorla, L. A. (2001). *The manual for the ASEBA school-age forms & profiles*. Burlington, VT: University of Vermont, Research Center for Children, Youth, and Families.

Bacharier, L. B., Strunk, R. C., Mauger, D., White, D., Lemanske, R. F., & Sorkness, C. A. (2004). Classifying asthma severity in children: Mismatch between symptoms, medication use, and lung function. *American Journal of Respiratory and Critical Care Medicine*, *170*, 426–432. https://doi.org/10.1164/rccm.200308-1178OC

Barnes, P. J. (2001). Th2 cytokines and asthma: An introduction. *Respiratory Research*, *2*, 64–65. https://doi.org/10.1186/rr39

Barnes, P. J. (2008). Immunology of asthma and chronic obstructive pulmonary disease. *Nature Reviews Immunology*, *8*, 183–192. https://doi.org/10.1038/nri2254

Bloom, B., Jones, L. I., & Freeman, G. (2013). Summary health statistics for U.S. children: National Health Interview Survey, 2012. *National Center for Health Statistics. Vital Health Statistics*.

Bowlby, J. (1973). *Attachment and loss: Vol. 2. Separation*. New York, NY: Basic Books.

Bowlby, J. (1982). *Attachment and loss: Vol. 1. Attachment*. New York, NY: Basic Books. (Original work published 1969)

Bowlby, J. (1988). *A secure base: Parent–child attachment and healthy human development*. New York, NY: Basic Books.

Brody, G. H., Ge, X., Conger, R. D., Gibbons, F. X., Murry, V. M., Gerrard, M., . . . Simons, R. L. (2001). The influence of neighborhood disadvantage, collective socialization, and parenting on African American children's affiliation with deviant peers. *Child Development*, *72*, 1231–1246. https://doi.org/10.1111/1467-8624.00344

Busse, W. W., & Lemanske, R. F. (2001). Asthma. *New England Journal of Medicine*, *344*, 350–362. https://doi.org/10.1056/NEJM200102013440507

Cassibba, R., van IJzendoorn, M. H., Bruno, S., & Coppola, G. (2004). Attachment of mothers and children with recurrent asthmatic bronchitis. *Journal of Asthma*, *41*, 419–431. https://doi.org/10.1081/JAS-120033984

Cassidy, J., & Kobak, R. R. (1988). Avoidance and its relation to other defensive processes. In J. Belsky & T. Nezworski (Eds.), *Clinical implications of attachment* (pp. 300–323). Hillsdale, NJ: Erlbaum.

Cassidy, J., & Woodhouse, S. S. (2003). *The secure base scale-revised*. Unpublished manual.

Cassidy, J., Ziv, Y., Rodenberg, M., & Woodhouse, S. S. (2003, April). *Adolescent perceptions of parents: Associations with adolescent attachment (AAI) and interactions with parents*. In R. Kobak (Chair), Assessing attachment in middle childhood and adolescence: Toward a multimethod approach. Symposium conducted at the biennial meeting of the Society for Research in Child Development, Tampa, FL.

Chen, E., Bloomberg, G. R., Fisher, E. B., & Strunk, R. C. (2003). Predictors of repeat hospitalizations in children with asthma: The role of psychosocial and socioenvironmental factors. *Health Psychology*, *22*, 12–18. https://doi.org/10.1037/0278-6133.22.1.12

Chen, E., Hanson, M. D., Paterson, L. Q., Griffin, M. J., Walker, H. A., & Miller, G. E. (2006). Socioeconomic status and inflammatory processes in childhood asthma: The role of psychological stress. *Journal of Allergy and Clinical Immunology*, *117*, 1014–1020. https://doi.org/10.1016/j.jaci.2006.01.036

Chen, E., & Schreier, H. M. C. (2008). Does the social environment contribute to asthma? *Immunology and Allergy Clinics of North America*, *28*, 649–664. https://doi.org/10.1016/j.iac.2008.03.007

Chen, E., Shalowitz, M. U., Story, R. E., Ehrlich, K. B., Manczak, E. M., Ham, P. J., . . . Miller, G. E. (2017). Parents' childhood socioeconomic circumstances are associated with their children's asthma outcomes. *Journal of Allergy and Clinical Immunology*, *140*, 828–835. https://doi.org/10.1016/j.jaci.2016.11.040

Chowdhury, F., Williams, A., & Johnson, P. (2009). Validation and comparison of two multiplex technologies, Luminex and Mesoscale Discovery, for human cytokine profiling. *Journal if Immunological Methods*, *340*, 55–64. https://doi.org/10.1016/j.jim.2008.10.002

Diamond, L. M., & Hicks, A. M. (2005). Attachment style, current relationship security, and negative emotions: The mediating role of physiological regulation. *Journal of Social and Personal Relationships*, *22*, 499–518. https://doi.org/10.1177/0265407505054520

Dykas, M. J., Ziv, Y., Woodhouse, S. S., & Cassidy, J. (2007). *Internal working models of attachment in adolescence: How do adolescent attachment organization, representations, and styles relate to one another and to adolescent-parent interaction?* Unpublished manuscript.

Ehrlich, K. B., Miller, G. E., & Chen, E. (2015). Family functioning, eosinophil activity, and symptoms in children with asthma. *Journal of Pediatric Psychology*, *40*, 781–789. https://doi.org/10.1093/jpepsy/jsv045

Ehrlich, K. B., Miller, G. E., Jones, J. D., & Cassidy, J. (2016). Attachment and psychoneuroimmunology. In J. Cassidy & P. R. Shaver (Eds.), *Handbook of attachment: Theory, research, and clinical applications* (3rd ed., pp. 180–201). New York, NY: Guilford.

Eisenberger, N. I., Inagaki, T. K., Mashal, N. M., & Irwin, M. R. (2010). Inflammation and social experience: An inflammatory challenge induces feelings of social disconnection in addition to depressed mood. *Brain, Behavior, and Immunity*, *24*, 558–563. https://doi.org/10.1016/j.bbi.2009.12.009

Groh, A. M., Fearon, R. M. P., van IJzendoorn, M. H., Bakermans-Kranenburg, M. J., & Roisman, G. I. (2017). Attachment in the early life course: Meta-analytic evidence for its role in socioemotional development. *Child Development Perspectives*, *11*, 70–76. https://doi.org/10.1111/cdep.12213

Jones, J. D., Ehrlich, K. B., Brett, B. E., Gross, J., Mohr, J., Hopper, E., . . . Kemeny, M. (2017). African American adolescents' perceptions of parental secure base support predict serum levels of C-reactive protein 20 years later. *Journal of Social and Personal Relationships*, *34*, 1168–1185. https://doi.org/10.1177/0265407516670532

Juniper, E. F., Guyatt, G. H., Feeny, D. H., Ferrie, P. J., Griffith, L. E., & Townsend, M. (1996). Measuring quality of life in children with asthma. *Quality of Life Research*, *5*, 35–46. https://doi.org/10.1007/BF00435967

Kaugars, A. S., Klinnert, M. D., & Bender, B. G. (2004). Family influences on pediatric asthma. *Journal of Pediatric Psychology*, *29*, 475–491. https://doi.org/10.1093/jpepsy/jsh051

Kobak, R. R., Cole, H. E., Ferenz-Gillies, R., Fleming, W. S., & Gamble, W. (1993). Attachment and emotion regulation during mother-teen problem solving: A control theory analysis. *Child Development*, *64*, 231–245. https://doi.org/10.1111/j.1467-8624.1993.tb02906.x

Kobak, R. R., & Duemmler, S. (1994). Attachment and conversation: Toward a discourse analysis of adolescent and adult security. In K. Bartholomew & D. Perlman (Eds.), *Advances in personal relationships* (Vol. 5, pp. 121–149). London, UK: Jessica Kingsley.

Marin, T. J., Chen, E., Munch, J. A., & Miller, G. E. (2009). Double-exposure to acute stress and chronic family stress is associated with immune changes in children with asthma. *Psychosomatic Medicine*, *71*, 378–384. https://doi.org/10.1097/PSY.0b013e318199dbc3

McQuaid, E. L., Walders, N., Kopel, S. J., Fritz, G. K., & Klinnert, M. D. (2005). Pediatric asthma management in the family context: The Family Asthma Management System Scale. *Journal of Pediatric Psychology*, *30*, 492–502. https://doi.org/10.1093/jpepsy/jsi074

Miller, G. E., Chen, E., & Cole, S. W. (2009). Health psychology: Developing biologically plausible models linking the social world and physical health. *Annual Review of Psychology*, *60*, 501–524. https://doi.org/10.1146/annurev.psych.60.110707.163551

Mrazek, D. A., Casey, B., & Anderson, I. (1987). Insecure attachment in severely asthmatic preschool children: Is it a risk factor? *Journal of the American Academy of Child & Adolescent Psychiatry*, *26*, 516–520. https://doi.org/10.1097/00004583-198707000-00009

Nachmias, M., Gunnar, M., Mangelsdorf, S., Parritz, R. H., & Buss, K. (1996). Behavioral inhibition and stress reactivity: The moderating role of attachment security. *Child Development*, *67*, 508–522. https://doi.org/10.1111/j.1467-8624.1996.tb01748.x

Nathan, R. A., Sorkness, C. A., Kosinski, M., Schatz, M., Li, J. T., Marcus, P., . . . Pendergraft, T. B. (2004). Development of the asthma control test: A survey for assessing asthma control. *Journal of Allergy and Clinical Immunology*, *113*, 59–65. https://doi.org/10.1016/j.jaci.2003.09.008

Oppenheim, D., Koren-Karie, N., & Sagi-Schwartz, A. (2007). Emotion dialogues between mothers and children at 4.5 and 7.5 years: Relations with children's attachment at 1 year. *Child Development*, *78*, 38–52. https://doi.org/10.1111/j.1467-8624.2007.00984.x

Pietromonaco, P. R., Uchino, B., & Dunkel Schetter, C. (2013). Close relationship processes and health: Implications of attachment theory for health and disease. *Health Psychology*, *32*, 499–513. https://doi.org/10.1037/a0029349

Puig, J., Englund, M. M., Simpson, J. A., & Collins, W. (2013). Predicting adult physical illness from infant attachment: A prospective longitudinal study. *Health Psychology*, *32*, 409–417. https://doi.org/10.1037/a0028889

Romagnani, S. (2000). The role of lymphocytes in allergic disease. *Journal of Allergy and Clinical Immunology*, *105*, 399–408. https://doi.org/10.1067/mai.2000.104575

Schatz, M., Sorkness, C. A., Li, J. T., Marcus, P., Murray, J. J., Nathan, R. A., . . . Jhingran, P. (2006). Asthma control test: Reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *Journal of Allergy and Clinical Immunology*, *117*, 549–556. https://doi.org/10.1016/j.jaci.2006.01.011

Schore, A. N. (2001). Effects of a secure attachment relationship on right brain development, affect regulation, and infant mental health. *Infant Mental Health Journal*, *22*, 7–66. https://doi.org/10.1002/1097-0355(200101/04)22:1<7:AID-IMHJ2>3.0.CO;2-N

Schreier, H. M. C., & Chen, E. (2010). Longitudinal relationships between family routines and biological profiles among youth with asthma. *Health Psychology*, *29*, 82–90. https://doi.org/10.1037/a0018311

Shalowitz, M. U., Berry, C. A., Quinn, K. A., & Wolf, R. L. (2001). The relationship of life stressors and maternal depression to pediatric asthma morbidity in a subspecialty practice. *Ambulatory Pediatrics*, *1*, 185–193. https://doi.org/10.1367/1539-4409(2001) 001<0185:TROLSA>2.0.CO;2

Tobin, E. T., Kane, H. S., Saleh, D. J., Wildman, D. E., Breen, E. C., Secord, E., & Slatcher, R. B. (2015). Asthma-related immune responses in youth with asthma: Associations with maternal responsiveness and expressions of positive and negative affect in daily life. *Psychosomatic Medicine*, *77*, 892–902. https://doi.org/10.1097/PSY.0000000000000236

Woodhouse, S. S., Dykas, M. J., & Cassidy, J. (2009). Perceptions of secure base provision within the family. *Attachment & Human Development*, *11*, 47–67. https://doi.org/10.1080/14616730802500792

Woodhouse, S. S., Ramos-Marcuse, F., Ehrlich, K. B., Warner, S., & Cassidy, J. (2010). The role of adolescent attachment in moderating and mediating the links between parent and adolescent psychological symptoms. *Journal of Clinical Child and Adolescent Psychology*, *39*, 51–63. https://doi.org/10.1080/15374410903401096