

ENVIRONMENTAL DETERMINANTS

The effects of low-level environmental tobacco smoke exposure on pulmonary function tests in preschool children with asthmaChristina Valsamis, MD¹, Sankaran Krishnan, MD, MPH², and Allen J. Dozor, MD²¹Division of Pulmonology, Winthrop University Hospital, Mineola, NY, USA and ²Division of Pediatric Pulmonology, Department of Pediatrics, Maria Fareri Children's Hospital at Westchester Medical Center and New York Medical College, Valhalla, NY, USA**Abstract**

Objectives: Though parents of children with asthma smoke, they often avoid smoking in their homes or near their children, thus limiting exposure. It is not known if such low-level environmental tobacco smoke (ETS) results in measurable exposure or affects lung function. The objectives of this study were to measure urinary cotinine in preschool children with asthma, and to examine the relationship between low-level ETS exposure and pulmonary function tests (PFTs). **Methods:** Preschool children with asthma were enrolled. Parents completed questionnaires on ETS exposure and asthma control, urinary cotinine concentrations were measured and PFTs were compared between subjects with and without recent ETS exposure. **Results:** Forty one subjects were enrolled. All parents denied smoking in their home within the last 2 weeks, but 14 (34%) parents admitted to smoking outside their homes or away from their children. Fifteen (37%; 95%CI: 23–53) of the children had urinary cotinine levels ≥ 1 ng/ml, of which seven (17%; 95%CI: 8–32) had levels ≥ 5 ng/ml. FEV₁ and FEV_{0.5} were lower in subjects with a urinary cotinine level ≥ 5 ng/ml as compared to those with levels < 1 ng/ml or between 1 and 5 ng/ml; both at baseline and after inhalation of albuterol. Five of seven subjects with urinary cotinine levels ≥ 5 ng/ml had FEV_{0.5} less than 65% of predicted values. There were no significant differences in IOS measures. **Conclusions:** Despite parental denial of smoking near their children, preschool children may be exposed to ETS. Such low-level ETS exposure may affect lung function, possibly in a dose-dependent manner.

Keywords

Lung function, preschool children, tobacco smoke exposure

History

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Introduction

For many, if not most, patients with life-long asthma, symptoms begin in infancy and early childhood [1–4]. Genetic, environmental and lifestyle factors all play important roles [4–8]. The lungs of infants and young children are particularly susceptible to damage when exposed to environmental toxicants including environmental tobacco smoke (ETS) [9,10]. As a result, the effects of ETS exposure on childhood respiratory health are an area of great interest and extensive investigation [10–13]. ETS increases the prevalence of asthma exacerbations, worsens asthma control and increases risk for developing fixed airflow obstruction [10–12,14]. Maternal smoking has been shown to be associated with deficits in spirometry in school-aged children [14]. Many parents take precautions to smoke outside of their home or away from their children [15]. Smoking outdoors with the door closed has been shown to help limit exposure, but these children still had significant difference in urinary

cotinine concentrations compared to controls [15]. School-age children with high levels of smoke exposure compared to those with low-level exposure are more likely to have had moderate or severe asthma [16] and worse lung function [17,18]. A safe ETS exposure threshold has not been established, though urinary cotinine levels ≥ 1 ng/ml are unlikely to be due to exposure to nicotine from sources other than air, such as food [19–21].

The objectives of this study were to assess ETS exposure with measurement of urinary cotinine in preschool children whose parents only smoked outside or away from their children; and to compare pulmonary function tests in those with evidence for ETS exposure to those without. The hypotheses were that many preschool children with asthma whose parents only smoked outside would have measurable urinary cotinine levels; and their pulmonary function would be lower than non-ETS exposed age-matched children, possibly in a dose-dependent manner.

Methods**Subjects**

Patients 3–6 years of age referred to the pediatric pulmonary function laboratory with a physician diagnosis of asthma were

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enrolled. The diagnosis of asthma was based on typical asthma symptoms such as recurrent wheeze, cough and breathlessness resolving spontaneously or with an inhaled bronchodilator. Subjects were excluded if they had a primary respiratory diagnosis other than asthma, known cardiovascular disease, a neuromuscular disorder, musculo-skeletal deformities or a restrictive pulmonary defect. In addition, subjects were excluded if they had a history of premature birth (≤ 34 weeks gestation) or an acute exacerbation defined as asthma-like symptoms requiring oral corticosteroids, emergency visit or hospitalization during the prior 4 weeks.

Procedures

This study was approved by the Institutional Review Board. After obtaining informed consent, demographic data was obtained and subjects completed a validated smoking exposure questionnaire [22] and an asthma control questionnaire [23]. Urinary cotinine was determined by the direct ELISA method (Calbiotech Inc., Spring Valley, CA), which reflects exposure to nicotine within 24–36 h [19,26]. Cotinine levels were measured in duplicate, and the mean of the two values are reported as unadjusted concentrations (ng/ml) [19,24–26]. Spirometry and impulse oscillometry were performed in accordance with American Thoracic Society (ATS) and European Respiratory Society (ERS) guidelines [27]. Measurements were made before and at least 15 min after nebulization of 2.5 mg of albuterol via hand-held small volume nebulizer. Spirometry values were compared to age-appropriate reference equations [27–31]. Impulse oscillometry measurements (R_5 , R_{10} , R_{20} and X_5) were compared to reference values established by Frei et al. [32].

Data analysis

Subjects were stratified into three groups: urinary cotinine <1.0 ng/ml, 1–5 ng/ml and >5 ng/ml. The distributions of continuous variables were characterized by their median and interquartile range (IQR). Mann–Whitney U tests were used to test for the significance of differences in continuous variables between the ETS exposed and non-ETS exposed groups, and Fisher Exact Probability Tests were used to compare categorical variables. Two-tailed p values of <0.05 were considered significant.

Results

Forty-one subjects were enrolled. None of the parents reported smoking in the home or around their child within the last 2 weeks. Two (14.3%) subjects in the exposed group had also been exposed to maternal smoking during pregnancy. Fifteen (37%; 95%CI: 23–53) children had urinary cotinine levels ≥ 1 ng/ml, a level unlikely to be secondary to non-environmental exposure to nicotine [19–21,26]. Of these 15 children, 8 were between 1 and 5 ng/ml and 7 had levels greater than 5 ng/ml. Five (12%) had urinary cotinine levels ≥ 10 ng/ml. The highest urinary cotinine level was 32 ng/ml. Fourteen (34%) parents reported smoking since their child was born. About 50% of those children had urinary cotinine levels ≥ 1 ng/ml, compared to 30% of the children whose

parents denied any parental smoking after the child was born ($p = 0.04$).

Patient characteristics are described in Table 1. There were no significant differences between exposed and unexposed groups in age, height, weight, sex, race, ethnicity, history of atopy or family history of asthma. All subjects denied acute exacerbations in the proceeding 4 weeks. About 14 (54%) of the non-ETS exposed group and 14 (93%) of the ETS exposed group were on daily anti-inflammatory medications ($p = 0.02$).

Spirometry results are presented in Table 2. There were no significant differences in either $FEV_{0.5}$ or FEV_1 between children with urinary cotinine levels <1 ng/ml and children with urinary cotinine levels between 1 and 5 ng/ml. However, median $FEV_{0.5}$ and FEV_1 were lower for the group of subjects with urinary cotinine level >5 ng/ml than either of the other two groups (Figures 1 and 2). These differences were present both before and after inhaled albuterol. About 5 of 7 subjects with urinary cotinine levels ≥ 5 ng/ml had $FEV_{0.5}$ less than 65% of predicted values (data not shown). Impulse oscillometry results are in Table 3. There were no significant differences between the three groups.

Discussion

ETS exposure has been shown to adversely affect the respiratory health of children with asthma [9–17]. Passive smoking has been implicated in increasing bronchial responsiveness [33–35], increased frequency of emergency room visits [36,37], increased hospitalizations, and impairment of recovery after hospitalization for acute asthma [38,39]. Many smoking parents attempt to limit their children's ETS exposure by smoking only out of their homes [15]. While these efforts decrease exposure, this study confirms that their children are still being exposed, based on measureable urinary cotinine concentrations. Urinary cotinine, a specific and

Table 1. Patient characteristics.

	Urinary cotinine (<1 ng/ml)	Urinary cotinine (>1 ng/ml)	p
N	26	15	
Age (years)*	5.6 (5.0–5.9)	5.3 (4.4–5.6)	0.06
Height (cm)*	111.1 (107–118)	112 (104–118)	0.61
Weight (kg)*	19.3 (18.6–22.7)	20.0 (18.9–25.0)	0.44
Sex (female)	11 (42%)	3 (20%)	0.27
ACQ score*	0 (0–0.53)	0.50 (0.14–1.25)	0.05
Race			
White	20 (77%)	11 (73%)	1.0
Black	2 (8%)	4 (27%)	0.17
Asian	4 (15%)	0 (0%)	0.28
Ethnicity			
Hispanic	11 (42%)	6 (40%)	0.86
Non-hispanic	15 (58%)	9 (60%)	0.86
Positive atopy history	19 (73%)	9 (60%)	0.60
Positive family history	14 (54%)	7 (47%)	0.92
Controllers*	14 (54%)	14 (93%)	0.02
In-utero ETS exposure	4 (15%)	0 (0%)	0.29
Urinary cotinine (ng/ml)*	0 (0–0.15)	4.5 (1.95–11.5)	<0.0001
Urinary cotinine ≥ 10 ng/ml	0 (0%)	5 (33%)	0.004

Inhaled corticosteroids and/or montelukast **Median (interquartile range).

Table 2. Spirometry in preschool children with asthma.

	Groups			<i>p</i>		
	A	B	C	A versus B	B versus C	A versus C
Urinary cotinine <i>n</i>	<1 ng/ml 26	1–5 ng/ml 8	>5 ng/ml 7			
FEV _{0.5} (l)	0.86 (0.78–1.02)	0.92 (0.82–0.99)	0.55 (0.47–0.75)	0.77	0.04	0.048
% Predicted	94 (78–101)	87 (83–98)	59 (53–72)	0.89	0.021	0.014
FEV _{0.5} , post-albuterol	0.94 (0.87–1.17)	0.96 (0.89–0.98)	0.64 (0.56–0.81)	0.24	0.032	0.009
% Predicted	102 (81–112)	91 (84–96)	67 (63–85)	0.38	0.024	0.002
FEV ₁ (l)	1.11 (1.02–1.34)	1.19 (1.09–1.29)	0.78 (0.70–1.15)	0.58	0.082	0.119
% Predicted	103 (88–115)	99 (92–103)	78 (71–86)	0.026	0.074	0.026
FEV ₁ , post-albuterol	1.15 (1.02–1.34)	1.25 (1.19–1.40)	0.89 (0.79–1.24)	0.54	0.046	0.05
% Predicted	105 (98–118)	100 (98–110)	89 (83–89)	0.617	0.011	0.009

All values are expressed as medians (interquartile range).

Figure 1. Urinary cotinine levels and FEV_{0.5} (% predicted value) before and after inhaled bronchodilator. All values are expressed as median (interquartile range).

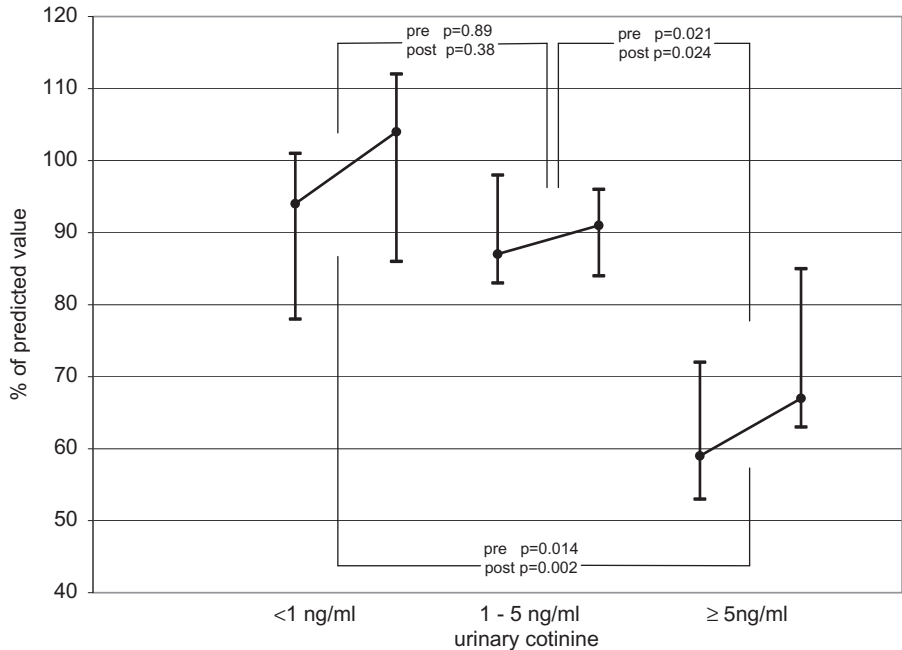


Figure 2. Urinary cotinine levels and FEV₁ (% predicted value) before and after inhaled bronchodilator. All values are expressed as median (interquartile range).

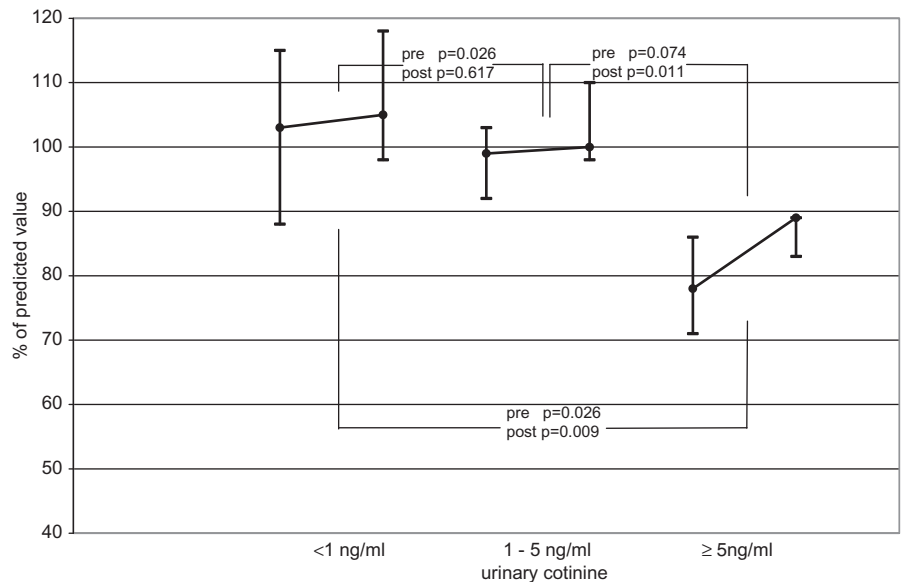


Table 3. Impulse oscillometry in preschool children with asthma.

	Groups			<i>p</i> value		
	A	B	C	A versus B	B versus C	A versus C
Urinary cotinine	<1 ng/ml	1–5 ng/ml	>5 ng/ml			
Sample size	26	8	7			
R ₅ , baseline	10.7 (9.5–11.9)	9.9 (9.6–10.7)	11.1 (9.0–12.5)	0.19	0.30	0.88
% predicted	100.1 (93.2–119.5)	97.5 (85.9–109.1)	100.7 (93.6–110.6)	0.23	0.36	0.93
R ₅ , post-albuterol	7.4 (6.6–8.6)	6.9 (6.4–8.0)	8.2 (7.3–9.9)	0.32	0.13	0.19
% predicted	73.2 (66.7–80.8)	63.9 (60.4–82.0)	77.6 (71.8–88.6)	0.36	0.17	0.22
R ₁₀ , baseline	8.3 (7.6–9.5)	8.1 (7.6–8.5)	7.5 (7.1–9.0)	0.18	0.47	0.56
% predicted	92.6 (83.7–101.9)	82.4 (79.0–98.6)	86.1 (81.0–89.7)	0.2	0.38	0.31
R ₁₀ , post-albuterol	6.3 (5.5–7.9)	6.2 (5.9–6.4)	6.9 (6.5–7.2)	0.56	0.16	0.16
% predicted	68.6 (61.8–78.4)	66.5 (61.4–75.9)	71.3 (69.3–79.6)	0.59	0.21	0.23
R ₂₀ , baseline	6.7 (6.1–7.9)	6.5 (6.0–6.9)	6.0 (5.9–7.3)	0.14	0.52	0.54
% predicted	92.4 (83.2–103.5)	85.6 (78.4–93.4)	84.5 (83.6–90.7)	0.16	0.47	0.37
R ₂₀ , post-albuterol	5.4 (4.7–6.3)	5.4 (5.2–5.8)	5.7 (5.5–5.9)	0.88	0.63	0.50
% predicted	74.7 (67.0–84.8)	70.8 (69.8–81.0)	75.5 (71.0–83.7)	0.92	0.72	0.67
R ₅ –R ₂₀ , baseline	3.6 (2.8–4.2)	3.3 (2.9–3.9)	4.2 (3.1–5.1)	0.38	0.31	0.42
R ₅ –R ₂₀ , post	2.0 (1.6–2.4)	1.4 (1.2–1.6)	2.5 (1.8–4.0)	0.25	0.09	0.32
X ₅ , baseline	–4.5 (–4.9 to –3.8)	–4.0 (–4.9 to –3.8)	–4.0 (–5.7 to –3.5)	0.86	0.53	0.74
% predicted	98.3 (84.4–108.5)	90.4 (77.9–100)	96.5 (73.4–122.6)	0.92	0.7	0.96
X ₅ , post	–3.1 (–3.5 to –2.6)	–2.6 (–3.1 to –2.5)	–3.3 (–4.4 to –2.3)	0.64	0.5	0.67
% predicted	67.7 (57.9–80.1)	59.8 (56.8–61.8)	77.8 (48.9–99.8)	0.74	0.68	0.90

All values are expressed as median (interquartile range).

major metabolite of nicotine with a half-life of approximately 20 h, has been established as a valid marker of recent exposure [19,21,26,40]. ETS exposure may be a combination of second-hand smoke and third-hand smoke, generally defined as exposure to tobacco smoke that previously settled onto furniture, clothes and inanimate objects and subsequently becomes re-suspended [41–44].

This study confirms that parental reports are not always reliable when used to screen for ETS exposure. Of the 14 subjects whose parents admitted only to outdoor smoking during the previous 2 weeks, 7 (50%) had urinary cotinine levels ≥ 1 ng/ml and 4 (28.6%) subjects had urinary cotinine levels ≥ 10 ng/ml. A safe threshold for ETS exposure has not been established. Based on urinary cotinine levels, 34% of preschool children in this study were exposed to ETS, since other sources of urinary cotinine such as nicotine in foods, are unlikely to result in levels ≥ 1 ng/ml [19–21]. However the subjects in this study were exposed to relatively low levels of nicotine, at least in the previous 24–36 h. Only one subject had a level >30 ng/ml, and one child had a level between 20 and 30 ng/ml. Adult active smokers (>10 cigarettes/day) have been reported to have mean urinary cotinine levels as high as 1100 ng/ml [45].

The relationship between low-level ETS exposure and lung function in preschool children has not been well studied. Cook et al. [18] studied the relationship between ETS exposure as measured by salivary cotinine and spirometry in a community based study of children 5–7 years of age, and found a small but significant decrement in lung function (difference of 6% in FEF₅₀ and 2% in FEV₁ between the highest and lowest quintiles for salivary cotinine) with increasing exposure. We detected what appears to be a dose-dependent difference in spirometry in preschool asthmatic children with low-level recent ETS exposure. There were no differences in impulse oscillometry measures.

There are a number of limitations to this study. The sample size was small. Children may be exposed to ETS from adults other than their parents. There may be unaccounted for confounding factors that affect lung function in this age group. There is difficulty in diagnosing asthma in this age range [45]. The subjects included in this study may be a mixture of phenotypes, and perhaps the relationship between ETS exposure and lung function would vary between specific asthma phenotypes [5]. This study was cross sectional, hence the effects of low-level ETS exposure on pulmonary function over time were not studied. Since ETS exposure affects pulmonary function in older children with asthma [14–17], perhaps the effects increase over time from cumulative exposure and may not be apparent in 3–6 year olds.

Conclusions

Based on urinary cotinine levels, preschool children with asthma whose parents insist they smoke outside of the home or away from their children are still exposed to tobacco smoke, albeit at low levels. Even low-level exposure to ETS may adversely affect lung function, possibly in a dose-dependent manner.

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Declaration of interest

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