Secondhand Tobacco Smoke Exposure and Severity of Influenza in Hospitalized Children

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Objective To assess whether children with influenza who are exposed to secondhand tobacco smoke (SHS) would have more severe illness than those not exposed.

Study design We abstracted charts from pediatric inpatients with confirmed influenza from 2002-2009 for demographics, medical history, and smoke exposure. Severity indicators included intensive care, intubation, and length of stay (LOS) in the hospital; potential confounding factors included demographics and the presence of asthma or chronic conditions. All χ^2, *t* tests, and regression analyses were run using SPSS v. 18.0.

Results Of 117 children, 40% were exposed to SHS, who had increased need for intensive care (30% vs 10%, $P < .01$) and intubation (13% vs 1%, $P < .05$), and had longer LOS (4.0 vs 2.4 days, $P < .01$). Children with chronic conditions and SHS exposure required more intensive care (53% vs 18%, $P < .05$) and had longer LOS (10.0 vs 3.5 days, $P < .01$) than children not exposed to SHS with chronic conditions. In multivariate analyses controlling for potential confounding factors, children with SHS exposure were 4.7 times more likely to be admitted to intensive care (95% CI 1.4-18.5) and had a 70% longer LOS (95% CI 12%-230%).

Conclusions Children with SHS exposure who are hospitalized with influenza have more severe illness. Efforts are needed to immunize this population against influenza, and eliminate children's exposure to SHS. *(J Pediatr 2013;162:16-21)*.

See editorial, p 8

Secondhand tobacco smoke (SHS) exposure is an important contributor to illness and premature death in pediatric patients.[1] Although only 18% of children live with someone who smokes in the home, biological markers of exposure identify 54% as being exposed[2]; these children may be exposed by parents who smoke outside[3] or other family members who smoke,[4] or even through incursions from neighboring apartments.[5] Children exposed to SHS are at greater risk for acute respiratory infections and asthma.[1,6] Respiratory illness is the leading cause of hospitalization for non-newborn children, and accounted for an estimated cost of $3 billion in 2006.[7]

Influenza is also a significant source of morbidity in children; more than 40% of pre-school children experience influenza,[8] and it is estimated that 20 000 children each year are hospitalized with influenza.[9] Thompson et al found that among children ages 0-5 years in the United States, there were nearly 5000 hospitalizations per year for pneumonia and influenza, and an additional 21 000 circulatory and respiratory condition hospitalizations per year associated with influenza from 1971-2001.[10] Despite the serious burden that influenza poses, and the significant effect of SHS on other respiratory illnesses, such as respiratory syncytial virus,[11] very little attention has been directed to the effect of SHS on children with influenza. One previous study did not find a statistically significant relationship between parental smoking and influenza in children in the first 4 years of life.[12] There have been studies exploring the biomedical risk factors for influenza in children, but these studies do not consider SHS exposure.[13,14]

Studies have examined the effect of tobacco smoke on influenza in the adult population, yielding mixed results. For example, 1 study of female Israeli Defense Force recruits found an OR of 1.44 for influenza infection among smokers, and that complications were also more common in smokers.[15] In another study, researchers found that among male Israeli Defense Force recruits, smokers had a 240% higher risk than non-smokers for influenza infection. There was also a dose-response relationship between the number of cigarettes smoked and complications, and authors concluded that 31.2% of the cases with influenza were attributable to smoking.[16]

ED	Emergency Department
LOS	Length of stay
PICU	Pediatric Intensive Care Unit
SHS	Secondhand tobacco smoke

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In order to assess the relationship between SHS and severity of illness in children hospitalized for influenza, we completed a retrospective chart review of pediatric patients admitted for influenza from 2002-2010. We hypothesized that children who were exposed to tobacco smoke would be more likely to be admitted to the Pediatric Intensive Care Unit (PICU), require intubation, and would have longer lengths of hospital stay.

Methods

The study took place at the Golisano Children's Hospital at the University of Rochester Medical Center in Rochester, New York. Potential subjects were identified first by generating a list of all patients ages 0-15 years who were assigned any discharge diagnosis of influenza (*International Classification of Diseases, 9th revision* 487.*) from 2002-2009; this resulted in a list of 171 patients. Charts for these visits were requested from medical records and were reviewed by a trained abstractor. Information collected included demographics (age, sex, and ethnicity) and insurance type. Clinical information abstracted included prior diagnoses or comorbid conditions, including asthma and prematurity, and medications prior to and during the hospital stay. Chronic conditions were defined as those disorders for which the Centers for Disease Control and Prevention recommends influenza vaccination: neurologic and neurodevelopmental conditions, chronic lung disease, heart disease, blood disorders, endocrine disorders, kidney disorders, liver disorders, metabolic disorders, and those causing weakened immune systems (eg, human immunodeficiency virus, AIDS).[17] As asthma has a strong relationship with both influenza and smoke exposure, we analyzed asthma as a separate category from the broader category of chronic conditions. In order to capture patients who had active asthma (rather than just a remote history of wheezing), patients were defined as having a preexisting diagnosis of asthma if they had a diagnosis of asthma in the admission notes (in the history of the present illness or medical history), and had albuterol and/or inhaled corticosteroids documented as home medications.

SHS exposure was assessed from the chart. Three possible sources of exposure documentation were used. Emergency Department (ED) providers have a standard section in their social history to document "smoking, alcohol, or drugs"; the nursing admission form has had a question "Does anyone smoke in the house or around the patient" since 2007, and the residents are instructed to collect smoke exposure status as part of their social history. A prior study in our institution found that ED providers documented screening for SHS exposure 46% of the time, nurses 79% of the time, and pediatric residents 42% of the time; 93% of patients were screened by at least 1 provider. Of those screened, ED providers identified 18% as exposed, pediatric residents identified 38% as exposed, and nurses identified 12% as exposed; 46% of patients were identified as smoke-exposed by cotinine testing and/or parent report. Those with SHS exposure outside the home were least likely to be asked and identified as exposed.[18] In the current study, patients for whom no exposure information was available (n = 29) were excluded (**Figure**). When available, information on the source of exposure (inside or outside the house) was obtained; children were classified as SHS exposed if there was mention of any exposure, whether inside or outside.

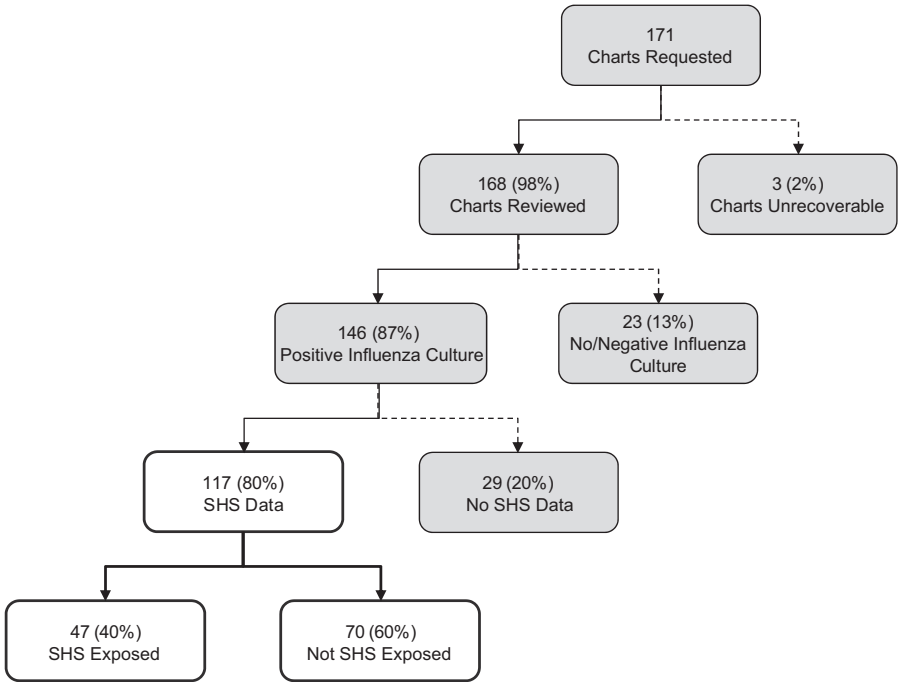

Figure. Charts reviewed with SHS data and positive influenza culture.

Table I. Demographic characteristics of pediatric inpatients with influenza

Variable	Overall (n = 117)	SHS exposed (n = 47; 40%)	Not SHS Exposed (n = 70; 60%)	*P* value
Sex				.91
Male	50%	51%	50%	
Female	50%	49%	50%	
Age–median y	2.6	2.8	2.6	.65
Race				.59
White	58%	53%	61%	
African-American	23%	28%	20%	
Other and unknown	19%	19%	19%	
Insurance				.24
Public	49%	55%	44%	
Private	51%	45%	56%	
Medications				
Anti-influenza	44%	40%	45%	.57
Antibiotics	68%	66%	70%	.65
Bronchodilator	36%	45%	30%	.11
Development of pneumonia	32%	32%	33%	.92
Bacterial infection	14%	26%	6%	<.01
Conditions				
Asthma	21%	26%	17%	.27
Chronic condition	29%	36%	24%	.17
Asthma and/or chronic conditions	46%	57%	39%	.05
Need for				
Intensive care	18%	30%	10%	<.01
Intubation	6%	13%	1%	.01
LOS–geometric mean (SD)	2.9 (11.8)	4.0 (18.1)	2.4 (2.1)	.011

PICU admission was defined as admission or transfer to the PICU at any time during the hospital stay. Intubation was defined as any documentation of endotracheal intubation during the admission. Length of stay (LOS) was abstracted from the insurance claim data summary for the hospital stay. Influenza status from discharge diagnosis was verified with laboratory data (rapid influenza antigen, polymerase chain reaction, or culture); patients without a positive influenza test by any of these methods were excluded (Figure). Several patients with documented positive cultures in the chart but without influenza typing (A or B) were included. Additional viral culture data was also noted. Pneumonia was defined as having any diagnosis of bacterial or other pneumonia in the chart; those with only a diagnosis of viral pneumonia were not included in this category. Patients were coded as having a bacterial infection if they had a diagnosis listed of bacteremia, sepsis, urinary tract infection, or a skin and soft tissue infection. Use of medications were noted, and 2 clinicians categorized all of the medications with 100% agreement; the primary categories were anti-influenza medications, antibiotics, and bronchodilator agents. The study was approved by the University of Rochester Research Subjects Review Board.

Analyses

χ^2, *t* tests, and Mann–Whitney U tests were used to determine bivariate differences between the smoke-exposed and non-smoke exposed groups. Geometrics means were used for LOS data to account for the skewed distribution of the variable. Demographic factors, significant variables from the bivariate analyses, and covariates of particular interest were included in the regression models; we were cautious to limit the number of independent variables because of concerns for overfitting. Logistic and negative binomial regression models were used to test for differences between groups while controlling for demographics and the presence of asthma and chronic conditions. Analyses were done using SPSS v. 18.0 (SPSS Inc, Chicago, Illinois).

Results

The Figure details the selection of our final sample of 117 patients. Demographic information is shown in Table I; 21% of the patients had a prior diagnosis of asthma, and 29% had a chronic condition. Four charts (3%) indicated both asthma and a chronic condition; these patients were included in both the asthma and chronic conditions groups. The most common non-asthma chronic conditions were cystic fibrosis (n = 3) and kidney transplant (n = 3). Of the children whose charts were included in the analysis, 40% were exposed to SHS, 18% were admitted to the PICU, 6% required intubation, and the median LOS was 2.0 days.

Children who were exposed to SHS were more likely to require intensive care (30% vs 10%, $P < .01$) and intubation (13% vs 1%, $P < .05$) than those children who were not exposed (Table I). Children exposed to SHS also had longer LOS than children not exposed to SHS (4.0 days vs 2.4 days, $P < .01$) (Table I). Additionally, those children with both a chronic condition and SHS exposure required intensive care more often (53% vs 18%, $P < .05$) and had longer LOS (18.8 days vs 4.4 days, $P < .01$) than children with chronic conditions, but without SHS exposure (Table II). Children with asthma and SHS exposure did not require intensive care or intubation more often, nor did they have a significantly longer LOS (Table II).

In a logistic regression analysis controlling for age, sex, insurance status, asthma, presence of bacterial infections, and chronic health conditions, the odds of being admitted to the PICU for children with SHS exposure were 4.7 (95% CI: 1.4-18.5) higher than children not exposed to SHS; the odds of being intubated were 8.8 higher, however this was not a significant difference (95% CI: 0.9-232.4) (Table III). SHS exposure was associated with a 70% longer LOS in a negative binomial regression analysis ($P < .01$) (Table III).

Discussion

Our study suggests that SHS exposure represents a significant risk to children who are hospitalized with influenza, resulting in a 5-fold increase in their chances of requiring admission to the PICU and increasing LOS by 70%. These data are consistent with evidence about the impact of SHS on severity in other respiratory illnesses, and in adults.

Table II. Severity indicators and smoke exposure in children with various conditions (n = 117)*

	Healthy† (n = 63)			Asthma (n = 24)			Chronic conditions (n = 34)		
	Smoke exposed (n = 20)	Not smoke exposed (n = 43)	*P* value	Smoke exposed (n = 12)	Not smoke exposed (n = 12)	*P* value	Smoke exposed (n = 17)	Not smoke exposed (n = 17)	*P* value
% Total	32	68		50	50		50	50	
% PICU	5	5	.95	50	17	.08	53	18	.03
% Intubation	5	0	.14	8	0	.31	29	6	.07
Geometric mean (SD) LOS	2.1 (1.5)	2.1 (1.2)	.85	4.1 (8.1)	2.2 (1.7)	.78	10.0 (27.6)	3.45 (3.4)	<.001

*Four children were included in both the asthma and chronic conditions categories.
†Children without asthma or chronic conditions.

This data has implications for the clinical care of children with influenza. ED and inpatient pediatric providers need to be aware of this association and assess SHS exposure for all patients being admitted for influenza. Understanding this relationship may help with risk-stratification. Our overall intensive care unit admission rate was high, but a similar rate was found in a chart review from Cincinnati.[19] Previous research has shown that many smoke-exposed children go unscreened, or are misidentified as having no exposure.[18] This represents a missed opportunity not only for risk assessment, but also for intervening with parents who smoke. Hospital admission for respiratory illness represents a "teachable moment" for parents,[20] and all inpatient care providers should be familiar with evidence-based techniques for smoking cessation intervention,[21] and with how to refer to the state Quitline system. Availability of free or low-cost nicotine replacement therapy in the hospital may not only encourage parents to quit smoking long-term, but also reduce their need to leave the child's bedside.

Table III. Regression analyses of risk factors for severe hospital course

	Intensive care unit admission		
		95% CI	
Variable	OR	Lower	Upper
SHS exposure	4.7	1.4	18.5
Race			
African-American	0.7	0.2	3.2
Other and unknown	2.6	0.5	12.8
Sex	0.3	0.1	0.9
Age	1.2	1.0	1.3
Insurance	0.5	0.2	1.7
Asthma	5.9	1.5	29.8
Chronic conditions*	6.4	1.6	29.8
Bacterial infections	1.6	0.3	6.9

	Intubation		
		95% CI	
Variable	OR	Lower	Upper
SHS exposure	8.8	0.9	232.4
Race			
African-American	1.2	0.0	19.2
Other and unknown	6.0	0.4	137.3
Sex	0.4	0.0	4.1
Age	1.2	0.9	1.5
Insurance	0.8	0.1	6.8
Asthma	0.9	0.0	13.2
Chronic conditions*	18.0	1.6	640.3
Bacterial infections	3.4	0.3	45.8

	LOS		
		95% CI	
Variable	IRR	Lower	Upper
SHS exposure	1.7	1.2	2.3
Race			
African-American	0.8	0.5	1.2
Other and unknown	1.3	0.9	2.0
Sex	1.0	0.7	1.3
Age	1.0	1.0	1.1
Insurance	0.9	0.6	1.2
Asthma	1.1	0.8	1.6
Chronic conditions*	2.9	2.0	4.1
Bacterial infections	1.6	1.1	2.4

IRR, incidence rate ratio.
*Other than asthma.

Children with chronic conditions seemed to be at particular risk for complications from influenza when exposed to tobacco smoke, and their mean LOS of 10 days is concerning. Children with chronic conditions represent some of the most vulnerable members of our society, and those with neurologic impairments may have no ability to leave a room while a parent is smoking, and no voice to express their discomfort at being exposed. We need vigorous efforts to counsel the caregivers of these children of risks of exposure, and to provide resources to help them quit smoking. Quality of life for a child with a disability should include smoke-free living.

Cost containment is a priority for our health care system; the mean total cost of an intensive care unit admission for influenza-related illnesses is 5 times more than admission to a general medical unit.[9] Overall, children who are SHS exposed are almost twice as likely to be admitted to the hospital in any year for lower respiratory tract infections,[22] and we have shown that when they are admitted, they stay almost twice as long. Emphasizing primary prevention through the elimination of children's exposure to SHS could result in significant cost savings to the health care system.

Unfortunately, children continue to be exposed, and continue to be at higher risk for complications from influenza. Yearly influenza vaccination is now recommended for all children, but amongst healthy children the rate of vaccination is still low: 32% for children aged 2-4 years and 21% for children aged 5-17 years.[23] The Centers for Disease Control and Prevention reported that by February of 2011, 49% of children aged 6 months-17 years had received the vaccine nationally since August of 2010.[24] Currently, children with asthma are

considered at higher risk, and are urged more strongly to be immunized; children exposed to SHS also should be considered high-risk based on our study. Several studies examining the pathophysiology of tobacco smoke exposure and viral illness suggest that suppression of interferon-γ and concomitant activation of Th2 responses could be at least in part responsible for increased illness severity.[25-27]

There are significant limitations to this study. As a chart review, we are only able to assess what was documented; this is particularly significant for the identification of SHS exposure. Based on our prior study of SHS exposure assessment, we know that about 30% of children who are not screened are in fact exposed to SHS,[18] and we do not know whether there is a bias towards screening for smoke exposure for children with a greater severity of illness. In this study, 20% of charts had no SHS exposure documentation; this is higher than the 7% found in our earlier study, and likely reflects the addition in 2007 of a structured nursing question on exposure. Even when documented, the SHS exposure assessment is only an estimate, and we cannot determine the actual level of exposure.

We are also not able to prove causation, only document a correlation; future prospective studies that utilize biomarkers of exposure will be able to determine whether this represents a true relationship, or the presence of an unmeasured confounder. As much as possible, we controlled for potential confounding factors that have been associated with increased severity of illness, or with SHS exposure, including race/ethnicity, having public insurance, and having a comorbid condition or asthma. Because our data is from a chart review, it is likely that there are limitations in the recorded diagnoses of asthma and other chronic conditions that potentially could have biased the results. Finally, our small number of subjects precludes us from more detailed analyses on specific chronic illnesses, or examining the role of specific medications. In particular, this limited our ability to examine the role of different factors in our regression model because of concern for overfitting. However, we feel that these data suggest an important risk for smoke-exposed children that needs to be investigated further.

Children exposed to SHS—nearly one-half in this study—who are admitted for influenza are at a significant risk for more severe illness and a longer hospital stay. Smoking parents of hospitalized children need to be counseled about smoke exposure reduction and offered resources to help them quit. ED and inpatient care providers should screen all pediatric patients for SHS exposure, and consider the potential increase in risk of severe disease when making decisions about placement and treatment. Aggressive efforts to eliminate children's exposure to SHS need to continue, both through addressing smoking behaviors among parents and through advocating for local and national policies that protect children from the unnecessary risks of SHS exposure. ■

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50 Years Ago in *The Journal of Pediatrics*

Feeding Value of Soy Milks for Premature Infants

Omans WB, Leuterer W, Gyorgy P. J Pediatr 1963;62:98-106

In an effort to test the acceptability and toxicity of protein-rich foods mandated by the World Health Organization and the United Nations Children's Fund, formulas prepared from soy protein were studied in rats and in premature infants. Premature infants were selected because of their rapid growth and prolonged hospitalization. Formulas (4 soy-based and 1 cow milk–based formulas) were evaluated in rats on the basis of the protein efficiency ratio (gram of weight gain per gram of test protein). Despite similar total protein contents, all soy formulas had lower protein efficiency ratio values than the cow milk–based formula. Clinical studies in premature infants were conducted over a 24-week period, encompassing both hospital and home monitoring. Significantly lower rates of growth (measured as the food efficiency ratio [weight gain per 100 mL formula]) and serum protein levels were observed in the infants fed soy-based formulas compared with those fed the cow milk–based formula. Infants fed soy-based formulas also manifest lower serum phosphorus and cholesterol values than those fed cow milk–based formula. There were more adverse effects in the soy-based group, such as diarrhea and perianal dermatitis. The study did note that differences among the soy-based formulas suggested that processing of the soy milk may be a factor. Nevertheless, the conclusion of the studies was that soy-based formula had an inferior biologic value to cow milk–based formula and that such soy-based formulas should not be used as a primary food source for infants.

In the 50 years since this report, neonatal nutritionists continue to remind us of the facts identified in this study but soy-based formulas remain available, accounting for nearly 25% of the formulas marketed in the US.[1] These studies indirectly identified the presence of phosphate binders and the hypocholesterolemic effects of soy milk. It is now routine manufacturing practice to add additional minerals (calcium, phosphorus, iron, zinc) to account for this intrinsic binding.

Thus, we do not recommend the use of soy milks for infants, and we especially never recommend these milks to premature infants. In contrast, adults may favor the hypocholesterolemic effects of a soy diet!

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