STUDY POPULATION. This population-based cohort included 5619 seven-year-old children in grades 1 and 2 recruited from a random sample of 283 public schools in the greater Toronto area.

METHODS. Cross-sectional data were collected on demographic characteristics, family history of atopy, smoke exposure, and outcome information until age 6 or 7 years by using validated questionnaires completed by a parent or guardian for all 5619 children. Further detailed longitudinal exposure data were obtained via telephone survey on a randomly selected case-control subset of 1497 children, one-half of whom had a reported history of asthma or wheezing. Statistical methods used to analyze associations included Cox proportional and discrete-time hazard survival analyses.

RESULTS. Increased risk of asthma development was associated with maternal smoking or home secondhand smoke exposure during pregnancy and first year of life, male gender, preterm birth, and maternal asthma. Breastfeeding at least 6 months conferred a protective effect. When adjusting for the aforementioned factors, maternal smoking or secondhand smoke exposure during pregnancy was associated with a 30% increase in adjusted hazard of childhood asthma development. This association persisted for secondhand smoke exposure alone during pregnancy as well as after adjusting for secondhand smoke exposure during the first year of life and for exposure from birth to 7 years.

CONCLUSIONS. The results of this study suggest that there is an increased risk of developing childhood asthma with maternal secondhand smoke exposure during pregnancy, regardless of the mother’s active smoking status during that time.

REVIEWER COMMENTS. This study is the first to evaluate the association between maternal secondhand smoke exposure during pregnancy and childhood asthma development. Previous studies evaluated maternal smoking status during pregnancy, and others assessed early-life exposures after birth. Such findings highlight the need for smoking cessation education not only for pregnant mothers but for all smokers in the home.


Justin M. Skripak, MD
Oradell, NJ

Persistent Effects of Maternal Smoking During Pregnancy on Lung Function and Asthma in Adolescents


PURPOSE OF THE STUDY. The study was conducted to determine if the negative effects of maternal smoking during pregnancy on respiratory health persist into adolescence and, if so, to identify a mechanism.

STUDY POPULATION. The study population included 1129 Australian children, age 14 years, seen for one of multiple scheduled follow-up visits as part of a birth cohort study.

METHODS. Clinical data were collected on current asthma status; serum was collected for total and allergen-specific IgE measurements and for cytokine measurements; and urine was collected for prostaglandin F2α, and eosinophil protein X measurements. Prenatal maternal smoking was determined by using an antenatal questionnaire for all participants and with urine cotinine measurements in some participants.

RESULTS. Prenatal exposure to maternal smoking was reported in 21%, and current smoke exposure was reported in 8%. Maternal smoking in pregnancy resulted in a significantly increased risk for current asthma, current wheeze, exercise-induced wheeze, and forced expiratory volume in 1 second/forced vital capacity <80%. However, there was no increased risk for atopy, current asthma medication use, or bronchial hyperresponsiveness. These associations were not altered when adjustments were made for various factors, including current lung function, specific IgE level, and cytokine and inflammatory markers.

CONCLUSIONS. Maternal smoking during pregnancy resulted in increased risk of asthma and wheezing at age 14 years. This increased risk was not due to increased atopic sensitization or reduced lung function at this age.

REVIEWER COMMENTS. This study is novel in that it assesses the effects of maternal smoking during the prenatal period on asthma and wheezing during adolescence. The findings suggest that prenatal counseling regarding smoking can be used to assist in the primary prevention of asthma.


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Relationship of Secondhand Smoke and Infant Lower Respiratory Tract Infection Severity by Familial Atopy Status


PURPOSE OF THE STUDY. The goal of this study was to establish atopic predisposition as a predictive factor to lower respiratory tract infection severity in infants with secondhand smoke (SHS) exposure.

STUDY POPULATION. Study patients were 451 mother–infant pairs enrolled in TCRI (Tennessee Children’s Respiratory
This longitudinal prospective study assessed familial atopic predisposition and severity of viral respiratory infections in infants with SHS exposure. Term infants with a birth weight ≥2275 g were enrolled from September to May of 2004 to 2008 when they presented with lower respiratory tract infection for an acute care visit to a single academic medical center.

METHODS. A questionnaire was used for assessment of patient demographic characteristics, familial atopy predisposition, and environmental exposures. In this case, familial atopy predisposition was determined on the basis of 2 factors: (1) a mother with self-reported atopy or allergen sensitization; or (2) atopy in a first-degree relative of the infant. Medical records were reviewed. Hospital length of stay (LOS) and bronchiolitis severity scores (BSS) were used to determine severity of lower respiratory tract infection. Multivariable regression models were then used to investigate the relationship of SHS exposure, bronchiolitis severity, and family atopy.

RESULTS. Of 451 infants with lower respiratory tract infection, more than one-half had SHS exposure, more than one-third had mothers with atopic disease, and more than two-thirds had familial atopy. Univariate analysis showed that SHS resulted in higher BSS. However, when considering maternal atopic disease and allergic sensitization as variables, this study did not find a statistically significant difference in BSS or LOS with SHS exposure. Furthermore, utilizing familial atopy as a predictor of BSS in the SHS exposure groups showed no statistically significant difference versus those with no familial atopy. However, SHS exposure did increase the LOS of those infants with familial atopy. This finding is in contrast to patients with no familial atopy, in whom SHS did not affect LOS.

CONCLUSIONS. SHS was linked to longer LOS, but not BSS, in infants with familial atopy.

REVIEWER COMMENTS. As physicians, we are often faced with the daunting task of smoke-cessation counseling, particularly for the benefit of children exposed to SHS. Studies such as these are often referred to by physicians in daily practice when counseling families regarding the need for parental smoking cessation. Unfortunately, this study is limited by parental reports of SHS that are likely to be underreported. Because this study describes increased LOS for infants with SHS and lower respiratory tract infection in those with familial atopy, it lays the groundwork for further studies that may explore the consequences of these findings on the long-term pulmonary health of children.

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Passive Smoking Impairs Histone Deacetylase-2 in Children With Severe Asthma

PURPOSE OF THE STUDY. The oxidative stress from tobacco smoke impairs histone deacetylase–2 (HDAC2) via phosphorylation of phosphoinositide-3-kinase (PI3K)/Akt activation, leading to corticosteroid insensitivity. This study tested the hypothesis that passive exposure to tobacco smoke is associated with reduced HDAC2 in alveolar macrophages in children with severe, refractory asthma.

STUDY POPULATION. The study population included children aged 8.5 to 13.5 years with severe asthma, already receiving inhaled corticosteroids plus a long-acting β-agonist.

METHODS. Bronchoalveolar lavage fluid was obtained from all children during bronchoscopy. Subjects were divided into those exposed to passive tobacco smoke (PS) and those not exposed to PS. Exposure was assessed by using parent surveys and was supported by measurement of cotinine levels in the saliva and urine. Fractional exhaled nitric oxide levels were also measured. HDAC2 expression and activity, Akt/HDAC2 phosphorylation levels, and corticosteroid responsiveness in alveolar macrophages were assessed.

RESULTS. Parental reports of smoking correlated with measurable cotinine levels in the urine and saliva of the children. PS exposure reduced HDAC2 protein expression and activity. PS exposure also reduced the inhibitory effects of dexamethasone of tumor necrosis factor α–induced CXCL8 release in the alveolar macrophages. Children exposed to PS had higher neutrophil counts and CXCL8 expression in bronchoalveolar lavage fluid and lower Asthma Control Test scores compared with those not exposed.

CONCLUSIONS. PS exposure in children impairs HDAC2 function via PI3K signaling activation. This finding agrees with previous studies in adults. The high levels of oxidative stress and their end products seem to induce corticosteroid insensitivity with dysfunction of HDAC2. This study supports the conclusion that PS exposure not only worsens asthma symptoms but induces a state of steroid resistance in an already difficult-to-control asthma population.

REVIEWER COMMENTS. It is well known that secondhand tobacco smoke exposure is related to exacerbation of asthma in children and can be a risk factor for persistent asthma in later childhood. This study shows the molecular basis for this finding in children with severe asthma and how PS exposure can induce steroid insensitivity. Patients with severe asthma are already difficult to treat, and steroid resistance makes it even more difficult. This finding highlights the need, even more so, for parental education regarding the effects of tobacco smoke exposure on their children with asthma.
### Relationship of Secondhand Smoke and Infant Lower Respiratory Tract Infection Severity by Familial Atopy Status
Grace T. Padron and Vivian Hernandez-Trujillo

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