Published in final edited form as:
Curr Allergy Asthma Rep. 2013 December ; 13(6): . doi:10.1007/s11882-013-0389-1.

Effects of Tobacco Smoke Exposure in Childhood on Atopic Diseases

Christina E. Ciaccio[1] and **Deborah Gentile**[2]

[1]Division of Allergy, Asthma & Immunology; Children's Mercy Hospital; Kansas City, Missouri, USA

[2]Division of Allergy, Asthma & Immunology, Allegheny Health System; Pittsburgh, Pennsylvania, USA

Abstract

Although the smoking prevalence in the United States continues to decline since the Surgeon General's first report in 1964, certain vulnerable populations continue to be disproportionately affected by the adverse consequences of tobacco smoke exposure. Children are particularly vulnerable to exposure and are likely to suffer from both short- and long-term adverse consequences after early life tobacco smoke exposure. An overwhelming amount of evidence supports an association between asthma development and tobacco smoke exposure, and evidence is mounting that tobacco smoke exposure may also increase risk of IgE sensitization. This manuscript will review the effects of tobacco smoke exposure in childhood on the development of asthma and allergic sensitization, and will review practical strategies to assist motivated parents with smoking cessation.

Keywords

Tobacco smoke; Secondhand smoke exposure; Asthma; IgE sensitization; Allergic sensitization; Smoking cessation; Food allergies; Allergic rhinitis; Childhood; Atopic disease; Nicotine replacement therapies; Atopic sensitization

Introduction

Although the smoking prevalence in the United States continues to decline since the Surgeon General's first report in 1964, certain vulnerable populations continue to be disproportionately affected by the adverse consequences of tobacco smoke exposure [1]. As they typically have little to no control over their environment, children are particularly vulnerable to exposure and are likely to suffer from both short- and long-term adverse consequences after early life tobacco smoke exposure. The incidence of acute respiratory infections, middle ear infections, and premature death are all known to increase when children are exposed to tobacco smoke [2]. In addition, an overwhelming amount of evidence supports an association between asthma development and tobacco smoke exposure.

Corresponding Author: Christina E. Ciaccio MD, Division of Allergy, Asthma & Immunology, 2401 Gillham Road, Kansas City, MO 64108, USA, ceciaccio@cmh.edu, Telephone: (816) 960-8885.

Compliance with Ethics Guidelines

Conflict of Interest

Christina E. Ciaccio has received grant support from Frontiers: Heartland Institute for Clinical and Translational Research. Deborah Gentile declares that she has no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

The effect of tobacco smoke on allergic sensitization is less clear, but evidence has been mounting that tobacco smoke exposure may also increase risk of IgE sensitization to food and certain indoor allergens, challenging the long-held belief that the effect of tobacco smoke on the immune system is strictly immunosuppressive.

This paper will briefly review the effects of tobacco smoke exposure in childhood on the immune system with particular attention to the development of asthma and allergic sensitization and will end with practical strategies to assist motivated parents with smoking cessation. A detailed review of the health effects of passive smoking was performed by Strachan and Cook between 1997 and 1999 and can be accessed in Thorax if further information is desired [3–11].

Tobacco Smoke Exposure in Childhood

Childhood tobacco smoke exposure occurs in three different ways, all of which may have unique consequences. The adverse health effects of active smoking or primary exposure have been recognized for decades. In fact, the study of the association between smoking and lung cancer is often credited as the launch of modern epidemiology [12]. Coronary artery disease, peripheral artery disease, stroke, cancer, and chronic obstructive pulmonary disease are all known consequences of smoking. These diseases seem more relevant to adults as they are the result of years of smoking; however, 88 % of adult smokers report starting before the age of 18. Unfortunately, nearly 50 % of high school children have reported smoking at least once in their lifetime, while 20 % of high school students are current smokers [1]. As health impact of lifelong smoking, on both the individual and their cohabitants, is staggering, this population of teenage smokers is a primary target of smoking cessation campaigns.

The adverse health effects of secondhand tobacco smoke exposure, also known as environmental tobacco smoke, have only been recognized since the 1970s. The extent of the health impact, however, has only been fully appreciated in the past several years as the effects of state and nationwide smoking bans have been analyzed. In Ireland, the first country to enact a nationwide smoking ban in workplaces, the health effects of the ban were almost immediately realized when a 17 % reduction in respiratory problems in nonsmoking pub workers was seen 1 year after the ban and a 38 % reduction in chronic lung disease mortality nationwide was seen less than 10 years after the ban [13, 14]. Small-for-gestational-aged births also decreased nearly immediately, an effect that has also been sustained throughout the post-ban period [15]. Similarly, after implementation of smoking legislation in Scotland, hospital admissions for asthma among children was decreased by over 18 % when it had been previously increasing by 5 % each year prior to the ban [16].

Coined in 2006, thirdhand smoke is a newly named but long since suspected public health problem which is defined by the contamination of tobacco smoke that lingers after the cigarette has been extinguished. This contamination may last for months on surfaces even after smoking in the immediate area has ceased [17]. The adverse respiratory effects of thirdhand smoke on respiratory health were first recognized when studies failed to find a benefit to children’s health when parents smoke exclusively outdoors [18]. This led investigators to believe that the chemicals left on the clothes of smoking parents was inhaled by their children when they returned indoors, leading to respiratory effects as damaging as inhaling environmental tobacco smoke. This suspicion has been validated recently with two independent studies. The first found that thirdhand smoke can react with ozone to form ultrafine particles that exacerbate asthma, while another found that thirdhand smoke can cause DNA damage in human cells [19–21]. These findings have lead to a new concern that children in schools actually suffer from the adverse effects of thirdhand smoke on the clothing of their friends whose parents smoke.

Adverse Effects of Tobacco Smoke Exposure on the Immune System

Tobacco smoke is a complex mixture of over 5,000 different chemicals; however, only a fraction have been measured and concentrations reported [22]. Of those measured, a recent paper found that almost 100 different components have an established human inhalation risk value and are considered hazardous to human health [22]. Nicotine, hydrocarbons, carbon monoxide, volatile organic compounds, and reactive nitrogen moieties are thought to be the primary components of tobacco smoke that modify the immune response. The affect of these chemicals after inhalation are not limited to local respiratory effects and target nearly every cell in the immune system. A major limitation in fully understanding the effects of individual components of tobacco smoke, however, is that each chemical not only interacts with each other in the environment but also have competitive effects on the immune system.

As one of the earliest recognized adverse effects of tobacco smoke was lung cancer, tobacco smoke was viewed for many years as having strictly immunosuppressive effect. The overall effect of chronic tobacco smoke exposure, however, is clearly far more complex than simply suppressing the immune response. Evidence is suggestive that while tobacco smoke largely suppresses the Th1 response, Th2 responses are also enhanced, particularly when exposure occurs during fetal development. This has led to the now accepted belief that tobacco smoke more accurately causes dysregulation, rather than suppression.

The respiratory epithelium and smooth muscle are the first lines of defense in the lung and are susceptible to direct toxic activity of the chemicals in tobacco smoke. Studies have shown that tobacco smoke both increases the permeability of the epithelium and weakens mucociliary clearance [23]. This effect facilitates allergen penetration across the epithelium and augments histamine release from subepithelial sensitized basophils [24]. Further, tobacco smoke exposure increases secretion of the proallergic cytokine, thymic stromal lymphopoietin (TSLP) in lung tissue [25–27]. TSLP is a cytokine that influences development of Th2 cells through upregulation of OX40 ligand in dendritic cells and is now considered to be critical in development of atopic responses [28].

The effects of tobacco smoke on other cells of the innate immune system and cells of the adaptive immune system have also been well studied in vitro. Alveolar macrophages are increased in number, produce more pro-inflammatory mediators, and have a reduced ability to phagocytose bacteria when exposed to tobacco smoke [29]. Likewise, NK cell cytotoxic activity and cytokine release is impaired by tobacco smoke [30]. Most interestingly, however, is the effect of tobacco smoke on dendritic cells. In addition to the effects of tobacco smoke on TSLP expression from dendritic cells mentioned above, studies suggest that tobacco smoke uniquely suppresses Th1 responses and induces Th2 responses, an effect that is most pronounced in utero [31, 32]. Providing further evidence that tobacco smoke is proallergic, studies have found that all immunoglobulins except for IgE, which is increased, are decreased in response to tobacco smoke. Interestingly, this effect is not seen when exposed to smokeless tobacco or nicotine patches [29, 33, 34].

Tobacco Smoke Exposure and Asthma

Although the literature is mixed as to its role in asthma pathogenesis, the association between tobacco smoke and asthma exacerbations and asthma severity is clear. Acute exacerbations of asthma have been shown to increase with exposure to tobacco smoke whether exposure is measured by report or cotinine levels [35, 36]. Likewise, FEV1 and FEV1/FVC decrease, while acuity of exacerbations, health care utilization, and bronchial hyperreactivity all increase with increased exposure to cigarette smoke, measured by either of the aforementioned parameters [35, 37].

Smoke-free laws that ban smoking in public places has provided proof of concept that decreasing tobacco smoke exposure will decrease the incidence of asthma exacerbation. As stated above, Scotland experienced a greater than 18 % decrease in hospitalizations for asthma after smoke-free legislation [16]. A similar reduction was seen in England after enactment of smoke-free legislation. While admissions for asthma were increasing be 2.2 % per year prior to legislation, hospital admissions for asthma immediately decreased by 8.9 % after smoke-free legislation. This was equivalent to 6,802 fewer admissions over a 3-year period [38].

Evidence does continue to mount in support of a causative effect of tobacco smoke exposure and the development of asthma. This evidence is now so compelling that the Surgeon General concluded in a 2006 report that a causal relationship between parental smoking and ever having asthma can be inferred [2]. Further, this effect is supported by evidence in all stages of human development. In utero exposure to tobacco smoke has been associated with lower lung function during infancy and an increased risk of asthma during the first 7 years of life [39, 40]. This effect also seems to last into adolescence for girls whose mothers smoked heavily during pregnancy [41]. Postnatal exposure to tobacco smoke has been shown to increase both the prevalence and incidence of asthma particularly when a child's mother or both parents smoke (OR 1.2–1.5, OR 1.1–1.3, respectively) [5]. Early life exposure also increases the risk of recurrent wheezing illness that is not diagnosed as asthma and is not sustained through childhood [3].

Tobacco Smoke Exposure and Atopic Sensitization

Few studies have been designed to investigate the influence of tobacco smoke exposure on allergic sensitization. The in vitro data discussed previously strongly support this hypothesis; however, the epidemiologic evidence is less clear. In 2001, Diaz-Sanchez et al. used a murine model to demonstrate the effect of secondhand tobacco smoke on allergic sensitization. This group was able to show an increase in eosinophils, IL-5, GM-CSF, and IL-2 and a decrease in IFNγ in bronchoalveolar lavage fluid after exposure to OVA and secondhand tobacco smoke and subsequent reexposure with OVA [42]. This group, therefore, concluded that secondhand tobacco smoke exposure is sufficient to induce sensitization.

In 1999, Kulig et al. found that children who were pre- and postnatally exposed to tobacco smoke had 2.3 times the odds of being sensitized to food allergens than unexposed children. Children who were only exposed postnatally still had 2.2 times higher odds of sensitization [43]. The same effect was not found for outdoor allergens in this study. The group concluded that tobacco smoke did serve as an adjuvant for sensitization to allergens in which the children were routinely exposed. A similar study was done by Lannero et al. in 1999. This study found an increased odd of sensitization to cats of 1.96, a 1.46 higher odds of sensitization to food, and a 3.24 higher odds of sensitization to *Cladosporium herbarum* [44]. As the discrepant findings may be due to the levels of allergen exposure in the studied population, our group repeated a similar study which used allergen levels as a covariate. We were unable to find an increase in sensitization to any indoor allergen, however (unpublished data). Food allergic testing was not performed by our group. As the data are conflicting and repeated in few populations, further studies are needed to better clarify the role of tobacco smoke exposure on allergic sensitization.

Practical Strategies to Assist Parents with Smoking Cessation

Health care providers have the ability to make a tremendous impact on smoking cessation. This is particularly true in pediatrics where parents accompany their child(ren) to regularly scheduled well visits as well as sick visits. Interestingly, the majority of smokers wish to

quit but many are never asked about their smoking addiction or given advice on cessation. Major reasons contributing to the failure to address smoking cessation include lack of time and lack of knowledge of medications and treatment. Unfortunately, less than a quarter of physicians report any formal training in smoking cessation, and only approximately two-thirds report feeling confident in prescribing smoking cessation medications. Additionally, the majority of physicians are unaware of the US Public Health Service Clinical Practice Guidelines for smoking cessation. The remainder of this section will assist health care providers in becoming aware of the guidelines and will provide useful information on smoking cessation strategies and treatments [45–47].

The US Public Health Service updated their guidelines entitled “Treating Tobacco Use and Dependence” in 2008. These guidelines stress the use of the 5 “As,” (ask, advise, assess, assist, and arrange) to standardize the care of all patients. The first step is to *ask* about tobacco use. This can easily be blended into the regular screening process by incorporating it into the measurement of vital signs. The second step is to *advise*. Many patients report that a physician’s advice to quit is an important motivator for smoking cessation. It has been reported that brief interventions of as short as 3 min can significantly affect smoking cessation rates in all populations. Additionally, the US Health Service guidelines recommend using advice that is clear, strong and personalized. The third step is to *assess* the willingness of the patient to quit smoking. If the patient is willing to try to quit, it is the role of the health care provider to *assist* (the fourth step) these patients. Ideally, the patient should be given a combination of therapy with counseling and medication, since this has been found to be the most effective method for sustained cessation. Brief counseling in the office and adding the adjunctive telephone quit line (1-800-QUIT-NOW) can be effective. More challenging patients may need to be referred to a specialist in the field of tobacco dependence for more intensive therapy. Patients need to be trained to recognize situation that put them at risk of smoking or relapse. Many smokers use nicotine as a drug to cope with life stressors and may have undiagnosed depression and/or anxiety disorders. At follow-up, it is important to provide constant reinforcement regardless of how long it has been since the last cigarette. For a patient who is not yet willing to set a quit date, it is important for health care providers to use motivational techniques and briefly discuss the harmful effects of smoking. Understanding why a patient smokes and his/her perceived value of smoking can help direct discussions at follow-up visits. Indeed, studies have shown that patients who were not willing to quit but received ongoing cessation counseling reported increased satisfaction with their health care. Consequently, the fifth step is to arrange follow-up care [21, 45, 48, 49].

Nicotine replacement therapies (NRTs), including gum, lozenge, inhaler, nasal spray, and transdermal patch have been shown in meta-analysis of randomized controlled studies to be efficacious in smoking cessation. Studies have shown that NRTs increase the odds of long-term cessation by 1.5- to 2-fold. NRTs are specifically designed to relieve some of the nicotine withdrawal symptoms and have also been found to serve as good adjuvants to the nicotine-free medications, including bupropion and varenicline [27, 50–54]. Bupropion is a heterocyclic antidepressant that has been specifically marketed for smoking cessation. It acts as a weak inhibitor of norepinephrine, serotonin, and dopamine uptake, and an antagonist of the nicotine receptor. Most physicians recommend setting a quit date for 1 week after initiation of therapy and treatment should be continued for 7–12 weeks. Six-month cessation rates increased from 17 33 % for smokers who took bupropion versus placebo. Bupropion is generally well tolerated and the most common adverse effects are dry mouth and insomnia [55, 56]. Varenicline is currently the most successful single-agent medication for smoking cessation. It is a partial agonist of the nicotine receptor. Varenicline has a proven efficacy profile, and the most common adverse effect is nausea, which may be decreased by using a 1-week lead-in titration schedule. A quit date should be planned at the completion of the

first week of treatment. The combination of NRTs with varenicline has been found to be effective in controlling urges and triggers [57, 58].

Conclusions

Despite the declining prevalence of smoking and increase in smoke-free legislation, tobacco smoke exposure remains a significant public health burden, particularly in young children who have no control over their environment. The data is conclusive that smoking, environmental tobacco smoke, and thirdhand smoke all negatively impact childhood respiratory health, likely playing a causative role in asthma and certainly capable of causing asthma flares. The evidence is also mounting that tobacco smoke exposure can lead to allergic sensitization, particularly to foods, which could lead to devastating consequences and a lifelong burden of disease. It is important for health care providers to positively impact upon smoking cessation because it directly affects the care they provide. Positive results can be achieved by screening, counseling, prescribing cessation medication, and arranging follow-up. Additionally, further public health policy and smoke-free legislation is needed in order to fully protect children from the effects of tobacco smoke exposure in all forms.

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