

EDITORIAL

Household smoking, maternal atopy and allergic sensitization in children: Is it all academic?

Key words: tobacco, allergy.

Despite the well-publicized health effects of passive smoking, many young children are still exposed to cigarette smoke in their home. Exposure to environmental tobacco smoke (ETS) often begins in utero, due to maternal smoking, and continues during childhood if parents or regular visitors smoke. Worldwide, the prevalence of smoking during pregnancy varies between less than 10% to over 30%, and although smoking among pregnant women and women of child-bearing age are decreasing in some countries, they are increasing in others.¹

Infants born to women who smoke during pregnancy are more likely to be born prematurely, have lower average birth weights and are small for gestational age compared with infants born to non-smoking women.¹ Children who are exposed to tobacco smoke in early life have increased risk of wheeze, respiratory infections and asthma, as well as impaired lung function.² These are well-established adverse health outcomes of early-life exposure to ETS. The effect of parental smoking on allergic sensitization and allergic disease in children, however, is less well understood.

The effect of ETS exposure on the development of allergy has been an area of study for many years, but the evidence for an association remains weak. Indeed, Strachan and Cook³ found no conclusive evidence for an increased risk of early-life exposure to parental smoking on allergic sensitization in children, and the results of studies published since then remain conflicting. Data from some studies demonstrate an increased risk of allergic sensitization due to parental smoking,^{4,5} others show no effect,^{6,7} while a few suggest that parental smoking is protective against sensitization.^{8,9} Factors such as the timing and extent of exposure and the age and type of sensitization have varied between studies and contribute to the ongoing uncertainty.

The effects of cigarette smoke exposure on sensitization may also be influenced by genetic susceptibility, and an inherited allergy risk (i.e. parental allergy) has shown to modify the association.^{4,5,8} In this edition of *Respirology*, Havstad *et al.*¹⁰ demonstrate that maternal allergy strongly influences the relationship between early-life exposure to cigarette smoke and allergic sensitization in young children (2–3 years). In this study, exposure to household smoke during pregnancy and the first month of life increased the odds of sensitization in children of mothers without a history of allergic disease but significantly reduced odds for children with allergic mothers.¹⁰ To some degree,

these findings are in agreement with previous studies^{5,11} but are in direct contrast with others.^{4,8} For example, both Keil *et al.*⁴ and Kuyucu *et al.*⁸ reported increased odds of Immunoglobulin E (IgE)-mediated sensitization in children exposed to ETS but only in those with a parental history of allergy. Interestingly, in the study by Kuyucu *et al.*,⁸ a protective effect of maternal smoking on allergic sensitization, although not stated, can be inferred for children of non-allergic mothers.

A plausible biological mechanism to support a protective effect of ETS against allergic sensitization is currently lacking. Although not conclusive, results from human and animal studies generally argue against such a finding. Active smoking by humans can suppress some T-helper type 1 (Th1) responses, facilitate Th2 inflammation and increase circulating IgE levels, while in murine models, ETS exposure can enhance allergic sensitization.^{12,13} Antenatal tobacco smoke exposure has shown to disrupt placental antioxidant function, which may affect early immune development, and has been associated with elevated cord blood IgE levels.¹⁴ Furthermore, maternal smoking has also shown to impair toll-like receptor (TLR) signalling (innate immunity) in neonates, and this relationship was further attenuated by maternal atopy.¹⁴ The authors suggested that smoking-induced impaired innate immunity may explain increased risk of respiratory infections during childhood and possibly also predispose to a Th2 bias.¹⁴ However, it remains to be demonstrated how any effect of smoke exposure on neonatal immune responses influence the subsequent development of allergic sensitization. Moreover, there are no well-supported explanations as to how maternal allergy may protect against the development of allergy in children exposed to cigarette smoke. It is a compelling issue, and since the epidemiological evidence is so equivocal, it is unlikely to be resolved unless a biologically plausible explanation can be established.

As with any epidemiological study, identifying and controlling for confounders and other risk factors are a major concern. This is particularly so when there may be systematic differences between exposure groups, as is often the case for groups with and without smoke exposure. In this study, the authors use propensity score (PS) methods to try to control for confounding bias by matching exposed and non-exposed on important baseline variables. In theory, if the baseline covariates can be balanced, the study will, to some degree, mimic a randomized control trial. This is a novel approach but, as the authors themselves acknowledge, does not by itself provide

the definitive answer to ongoing uncertainty surrounding parental smoking in childhood allergy. It cannot be assumed that the answers using this method are more robust than using more conventional regression adjustment, and it is often the case that similar effects are observed when using PS and conventional methods.¹⁵ However, new methods for assessing old problems, when correctly applied, should always be encouraged.

This area remains complicated due to a multitude of factors. Epidemiological studies need to continue to try to identify and control for confounding factors, and the attempt to do that in the study by Havstad *et al.*¹⁰ is commendable. A greater understanding of the role of factors such as genetic susceptibility, timing of exposure (pre- and/or postnatal), degree of exposure and allergic outcome is required. From a scientific point of view, resolving this issue is important. Understanding the relationship between parental smoking and allergic sensitization in children, the factors that influence the relationship and the underlying mechanisms may improve our understanding of both smoking-related disease and general developmental immunology. However, from a public health point of view, it could be argued that it is all academic. It is well established that exposure to ETS adversely affects the health of children, and translating current knowledge into an effective public health message remains the key challenge.

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