Third-hand smoke exposure and health hazards in children

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Introduction

Smoking still represents a huge public health problem. Approximately 1.1 billion people are current smokers worldwide and this figure is expected to rise to over 1.6 billion by the year 2025 [1]. Millions of children suffer the detrimental effects of passive smoking. An increasing number of countries have recently issued laws to regulate smoking in public places. Instead, homes remain a site where children are dangerously exposed to environmental tobacco smoke (ETS). The combination of tobacco smoke pollutants which remain in an indoor environment, the so-called ‘third-hand smoke’ (THS), represent a new concept in the field of tobacco control. THS consists of pollutants that remain on surfaces and in dust after tobacco has been smoked, are re-emitted into the gas-phase, or react with other compounds in the environment to form secondary pollutants. Indoor surfaces can represent a hidden reservoir of THS constituents that could be re-emitted long after the cessation of active smoking. Human exposure to THS pollutants has not yet been thoroughly studied. Infants and children are more prone to the risks related to THS exposure than adults because they typically spend more time indoors and have age-specific behaviours that may expose them to potential health hazards from THS. Further investigations are warranted to study the health effects of THS relevant to different exposure pathways and profiles. It would also be very important to evaluate how THS may affect the lung development through the in utero exposure during the pre-natal life. We aimed at reviewing recent findings published about THS, with special reference to the effects on children’s health.

What is Third-hand Smoke?

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Keywords: Environmental tobacco smoke, Children, Lung development, Asthma, Tobacco control, Indoor environment, Third-hand smoke.
Hence, the exposure risk to passive smoking does not end when a cigarette has been extinguished and may persist also in the absence of further smoking [5].

**Constituents and Transformation of THS**

The main constituents of THS are nicotine, 3-ethenylpyridine, phenol, cresols, naphthalene, formaldehyde and tobacco-specific nitrosamines. Physical and chemical transformations of tobacco smoke pollutants take place after their release during smoking. These reactions can occur in a range from few seconds to several weeks or months [5].

Nicotine is the most abundant organic compound emitted during smoking [6]. It has been demonstrated to deposit almost entirely on surfaces persisting for weeks to months, whereas most other tobacco smoke constituents showed more moderate sorptive tendency [5].

Moreover, nicotine can react with oxidant gases normally present in indoor environments (ozone, nitrous acid) to form nitrosamines (TSNAs), such as 1-([N-methyl-N-nitrosamino]-1-(3-pyridinyl)-4-butanal (NNA), 4-(methylnitrosamino)-1-(3-pyridinyl)-1-butanone (NNK) and N-nitrosonornicotine (NNN). These compounds are classified by the International Agency for Research on Cancer as lung carcinogens [7]. Due to their very low volatility, these carcinogens can persist indoors and on the human skin envelope: it is plausible that inhalation and ingestion of TSNA-loaded dust as well as dermal contact with contaminated surfaces are the main exposure pathways for such exposure [6].

At last, nicotine can react to form volatile compounds including formaldehyde, that is a known human carcinogen for which there is no safe level of exposure [8].

Thus, indoor surfaces can represent a hidden reservoir of THS constituents that could be re-emitted long after the cessation of active smoking [5].

Since infants are often in close contact with surfaces and dust and they have a higher respiration rate and a lower body weight than adults, even low doses of TSNAs may represent a long-term health hazard [6].

**The magnitude of the problem**

The chemistry and physics of tobacco combustion in indoor environments suggest that some THS constituents can remain for long periods after the actual smoking has taken place [5]. Possible repositories of THS are indoor surfaces such as walls, doors, curtains, carpet, upholstery, pillows, mattresses, clothes and even skin and hair [9] (table 2).

Nicotine has also been found to contaminate private homes of non-smokers formerly occupied by smokers [4]. Matt GE, *et al* [4] found that significant correlation between finger nicotine levels and urine cotinine levels determined in occupants of smoker homes are dangerous reservoirs of THS pollutants.

**Table 1. - Main differences between SHS and THS**

<table>
<thead>
<tr>
<th></th>
<th>SHS</th>
<th>THS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure route</td>
<td>Inhalation of side-stream and main-stream smoke</td>
<td>Inhalation, ingestion, dermal uptake of pollutants</td>
</tr>
<tr>
<td>Exposure time profiles</td>
<td>High levels over short intervals</td>
<td>Low levels over long periods</td>
</tr>
<tr>
<td>Features</td>
<td>Removal through ventilation</td>
<td>Persistence on indoor surfaces and human envelope</td>
</tr>
<tr>
<td>Repositories</td>
<td>Walls, doors, carpets, upholstery, pillows, curtains, mattresses, clothes, skin, hair</td>
<td></td>
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</tbody>
</table>

**Table 2. - Magnitude of THS exposure**

<table>
<thead>
<tr>
<th>Author</th>
<th>Duration of exposure</th>
<th>Place of exposure</th>
<th>Outcome</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Matt GE, <em>et al</em> [4]</td>
<td>Weeks</td>
<td>Homes of non-smokers formerly occupied by smokers</td>
<td>Significant correlation with finger nicotine levels and urine cotinine levels determined in occupants</td>
<td>Smoker homes are dangerous reservoirs of THS pollutants</td>
</tr>
<tr>
<td>Matt GE, <em>et al</em> [5]</td>
<td>Previous year before the study</td>
<td>Automobile cabin of smokers and non-smokers</td>
<td>High nicotine levels on surfaces of smoker cars</td>
<td>Significantly higher levels of nicotine in smoker cars than those from cars where smoking bans were imposed</td>
</tr>
<tr>
<td>Schick S, <em>et al</em> [8]</td>
<td>Previous years before the study</td>
<td>House of smokers at the time of the study</td>
<td>Significant correlation between nicotine concentration and the house age</td>
<td>Traditional cleaning methods cannot remove the long-standing pollutants effectively</td>
</tr>
</tbody>
</table>
by smokers. Even after several weeks, dust and surface nicotine levels are still higher than in non-smoker homes, with a significant correlation with finger nicotine levels and urine cotinine levels determined in occupants. Therefore, smokers’ homes represent dangerous reservoirs of THS pollutants to whom non-smokers are involuntary exposed [4].

Moreover, a recent study found that the smoking status of the occupants during the previous years is a stronger predictor of high nicotine levels in the house than smoking status at the time of the study. The authors also found a significant correlation between nicotine concentration and the age of the house. Similarly, it has been recently observed that the strongest predictor of house dust polycyclic aromatic hydrocarbons (PAHs) is the building age. Therefore, there is evidence that many pollutants accumulate in homes and traditional cleaning methods cannot remove them effectively [8].

The automobile cabin also represents a hazardous environment for non-smoker exposure. Recently, it has been demonstrated that there are high nicotine levels on surfaces of smokers’ cars, such as dashboards, upholstery and window glasses. These levels persist days after active smoking took place and are significantly higher than those from cars where smoking bans were imposed or from non-smoker cars [5].

Finally, there is some evidence that THS is detectable on smoker hands with the possibility to spread THS pollutants to other persons or objects [5].

The presence of THS constituents in the air, in dust, and on surfaces of indoor environments accounts for different possible exposure routes. In fact, in addition to exposure to volatile compounds re-emitted from contaminated surfaces through inhalation, there are other potential exposure routes for the less volatile THS components, such as dermal contact and ingestion of dust loaded with THS constituents [9].

Comparing THS with SHS and active smoking, there is evidence that it involves different time profiles of exposure (low level of exposure over long periods vs high levels over short intervals), different kinds of pollutants with different concentrations in different media (air, surfaces and dust) and various kinds of exposure route (inhalation, dermal contact and ingestion). Thus, exposure to THS implies health risks that are not directly, or exclusively, associated with tobacco smoke [5].

All these findings suggest that THS is ubiquitous since it is not limited to the space in which tobacco was smoked and it may represent a serious danger for human health.

Health implications in children

Human exposure to THS pollutants has not been thoroughly studied to date. Hence, it is not yet possible to fully evaluate what are the health hazards from the exposure to THS. However, it is possible to consider the detrimental effects on human health of some of the known THS compounds. In fact, it is well known that nicotine has a role in carcinogenesis, has adverse effect on vascular system and may promote inflammation through oxidative stress, as well as it may alter brain and lung development in children. It is also to point out that nicotine can react with other pollutants to form new compounds, such as TSNAs and formaldehyde, known as potent human carcinogens. Moreover, other tobacco smoke constituents can have detrimental effects on health: PAHs, particularly benzo[a]pyrene, are carcinogenic; oxidant gases can promote oxidant damage and inflammation through the production of free radical species and can trigger allergic symptoms and asthma [5]. At last, a correlation between low levels of tobacco smoke markers and cognitive deficits in children has been shown, suggesting that some compounds in tobacco smoke may be neurotoxic, even at extremely low levels [3].

Undoubtedly, infants and children are more prone to the THS exposure-related risks than adults. In fact, they typically spend more time indoors and have age-specific behaviors, i.e. crawling and ingesting non-food items, that may expose them to potential health hazards from THS (table 3). Moreover, children are more sensitive than adults to pollutants in house dust for several factors: increased respiration relative to body size (that determines a higher dust ingestion rate than adults); physiologic immaturity of respiratory and immunologic systems; low metabolic capacity; longer life expectancy [4].

The mechanisms underlying pre-natal and post-natal lung effects of passive smoking exposure are likely to be different. Evidence exists about tobacco smoke’s ability to elicit epigenetic changes that cause direct or indirect oxidative stress. A putative mechanism for an interaction between epigenetic modulation and environment, as identified in asthma studies, might result in increased risk for children exposed to maternal smoke [10]. Moreover, there is evidence that in utero smoke exposure may have a larger role in lung function impairment than postnatal exposure. The direct effects of maternal smoking on lung development are mainly due to the smoke components that are transferred across the placenta. Nicotine is able to cross the human placenta with minimal transformation into its metabolite “cotinine” and accumulates in amniotic fluid, several fetal tissues (including the lungs) and in maternal milk. Therefore, the fetus is exposed to even higher levels than those of the smoking mother [11].

It is well known that maternal tobacco smoking during pregnancy causes increased risk of wheezing, asthma and reduced lung function in offspring, independently from smoke exposure during postnatal life. Several studies have also demonstrated that maternal smoking during pregnancy may alter lung development in offspring. In some animal models, it has been shown that in utero smoke exposure contributes to alveolar remodeling increasing collagen deposition around large airways and vessels in offspring [12]. Furthermore, in children who died of sudden infant death syndrome (SIDS), at autopsy the inner airway wall was found thicker in those from smoking
More recently, Rehan and co-workers demonstrated that THS exposure at home can affect children’s lower respiratory system more exposed and have an increased risk of suffering from both wheeze and bronchitis symptoms, compared to males of similar age [15].

A recent study conducted by Jung and co-workers demonstrated that THS exposure at home can affect children’s lower respiratory system increasing cough morbidity. The Authors also noted a linear trend in the symptoms frequency among three groups according to the degree of ETS exposure (non-smoking, SHS and THS group). In fact some symptoms, including cough and nasal symptoms, were highest in the SHS group, followed by the THS and the non-smoking groups. Therefore, even if less than SHS, THS has substantial effects on children’s respiratory system [16].

It has been previously demonstrated that urine cotinine levels of children living in homes with strict smoking bans are significantly lower in homes without such policies [9]. Matt and coworkers found that ETS exposure (measured by cotinine levels in infant urine) were 5-7 times higher in homes without such policies versus non-smoking mothers [13]. This cumulative evidence is suggestive for airway remodeling due to in utero smoke exposure that may cause impaired lung function in children. The decreased alveolar surface area may compromise the gas-exchange capacity of the lungs, reducing tissues oxygenation. The persistent reduction in vessel density, as a result of smoke exposure during lung development, may have long term effects, such as a reduced exercise capacity and a poor tolerance to respiratory infections [12].

In addition, Blacquière recently demonstrated that smoking during pregnancy in mice is associated with increased goblet cell hyperplasia and larger number of House Dust Mite-induced neutrophils and mast cells. These different aspects of remodeling may significantly contribute to the increased airway hyper-responsiveness to the allergic stimulus observed in adult mice [14].

Moreover, using a biological model of lung development, Rehan found that in utero smoke exposure alters the specific communications between epithelium and interstitium, provoking the transdifferentiation of lung lipofibroblasts to myofibroblasts, i.e. the cellular hallmark of chronic lung diseases, including asthma. Since alveolar type II cells hyperplasia and abnormal differentiation have been reported in animal models of in utero smoke exposure, it is plausible that these findings might explain the long-term pulmonary effects (including the increased predisposition to asthma) in in utero smoke exposed children [11].

Table 3. Thirdhand smoke exposure and health hazards in children

<table>
<thead>
<tr>
<th>Author</th>
<th>Route of exposure</th>
<th>Outcome</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elliot J, et al [13]</td>
<td>Pre-natal exposure in utero</td>
<td>Increased inner airway wall thickness at autopsy in children died of SIDS (a) from smoking mothers vs in those from non-smoking mothers</td>
<td>Airway remodeling due to in utero smoke exposure may cause impaired lung function in children</td>
</tr>
<tr>
<td>Kabir Z, et al [15]</td>
<td>Post-natal exposure in cabin car</td>
<td>Increased risk of suffering from both wheeze and bronchitis symptoms in exposed females</td>
<td>Smoking in a car can be 23 times more toxic due to the limited space</td>
</tr>
<tr>
<td>Jung JW, et al [16]</td>
<td>Post-natal exposure in home</td>
<td>Increased cough morbidity in exposed children</td>
<td>THS exposure at home can affect children’s lower respiratory system</td>
</tr>
<tr>
<td>Matt GE, et al [17]</td>
<td>Post-natal exposure in home</td>
<td>Increased cotinine levels in infants from households of smokers smoking outdoors vs in those from households of non-smokers</td>
<td>Smoking outside the home and away from the infant does not completely protect a smoker’s infant from ETS exposure</td>
</tr>
<tr>
<td>Thomas JL, et al [18]</td>
<td>Post-natal exposure in home</td>
<td>Iso-NNAL not found in children’s urine sample, probably because it is less readily formed from NNA</td>
<td>No biomarker yet available to evaluate THS exposure in humans</td>
</tr>
</tbody>
</table>

(a): Sudden Infant Death Syndrome.
in households of smokers trying to protect their infants by smoking outdoors than in households of non-smokers. ETS exposure were 3-8 times higher in households of smokers who exposed their infants to ETS by smoking indoors than in households of smokers trying to protect their children by smoking outdoors. This suggests that smoking outside the home and away from the infant reduces but does not completely protect a smoker’s infant from ETS exposure [17]. In a recent study by Thomas and coworkers, it has been attempted to detect iso-NNAL (1- (methylnitrosamino)-1-(3-pyridyl)butan-4-ol, a metabolite of NNA) in the urine of children living in homes with smokers. iso-NNAL was not detected in any urine sample, probably because this metabolite appears to be less readily formed from NNA so that the low extent of formation could have limited the ability to detect it in urine [18]. However, since currently very little is known about actual health risks attributable to THS, it is important to underscore the necessity to develop biomarkers of its exposure, especially for children.

**Conclusion**

Many studies clearly demonstrated that active and SHS smoking do have serious effects on children’s health. Instead, there is a lack of studies of THS exposure, either in adults or in children. With the limited evidence available to date it is impossible to assess the exact role of THS in determining health outcomes in exposed people.

Hence, further investigations are warranted to study the health effects of THS relevant to different exposure pathways (inhalation, dermal contact, dust ingestion) and exposure profiles (short and long term). It would also be very important to evaluate how THS may affect the lung development through the in utero exposure during the prenatal life. In this context, it could be really interesting to validate biomarkers of exposure and tissue damage caused by THS, especially for use in children [5].

Surprisingly, there is no awareness on how can THS be a serious danger for human health. A survey conducted by Winickoff et al demonstrated that only 65.2% of non-smokers and 43.2% of smokers believe that THS is harmful to children [3]. Moreover, a survey of pediatricians showed that only 13% always asked about passive smoking exposure at visits for ear infections and 33% always gave advice to create a smoke-free home [19].

Protection of children from the detrimental effects of passive smoking has to become a high public health priority. In a recent study by Pellegrini et al it has been demonstrated a significant trend toward reduced exposure to ETS in adolescents, due to the implementation of smoke-free legislation and information campaign against smoking [20]. Educating adults about health hazards related to children THS exposure may be useful to increase public awareness of the problem and ensure a smoke-free environment for children [3].

In this context, further studies are warranted to investigate the effectiveness of the different policies aimed to protect children from exposure to passive smoking. Furthermore, in order to understand which interventions (campaigns, programs, routine clinical practice) could improve the strategies for tobacco control and promote health education a road map planning could be strongly advised (table 4).

**References**


