The relationship of early-life household air pollution with childhood asthma and lung function

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Abstract

The increase in childhood asthma over the past few decades has made it an important public health issue. Poor lung function growth associated with some phenotypes of asthma compounds its long-term impact on the individual. Exposure to early-life household risk factors is believed to be linked with respiratory health while infants’ lungs are still developing. This review summarises epidemiological studies and mechanistic evidence focusing on the detrimental effects of early-life household air exposures on the respiratory health of children, in particular effects on asthma and lung function. Many early-life household air exposures, including tobacco smoke, gases from heating and cooking, mould/dampness and cleaning products are associated with childhood asthma development and lung function growth. These exposures may alter structural and mechanical characteristics of infants’ lungs and contribute to deficits in later life. In addition, some risk factors, including tobacco smoke and cleaning products, can transmit effects across generations to increase the risk of asthma in subsequent generations. This review supports the hypothesis that risks of asthma and accelerated lung ageing are established in early life. The timing of exposure may be critical in the pathogenesis of respiratory diseases, in terms of future risk of asthma and reduced lung function in adults.

Introduction

Asthma is responsible for a significant health burden in children. Asthma symptoms are experienced by 14% of children worldwide. The highest prevalence of recent wheeze (>20%) was observed in the English-speaking countries of Europe, North America and Australia, as well as parts of Latin America [1]. Phase 3 of the International Study of Asthma and Allergies in Childhood (ISAAC) found that the burden of asthma was greatest for children aged 10–14 years, and it was the most common chronic disease in this age group [2]. Although a large proportion of children with asthma/wheeze in early life go into remission, some asthma persists into adulthood [3]. Compared to doctor-diagnosed late-onset asthma (after the age of 3 years), children with early-onset asthma (up to and including the age of 3 years) are more likely to have persistent respiratory symptoms into later childhood [4] and even adulthood [5]. The characteristic pathological features of asthma, namely increased reticular basement membrane thickness and eosinophilic inflammation, can occur in very young children (aged 1–3 years) with recurrent wheeze [6]. Therefore, exposure to adverse early-life risk factors may not only influence asthma development, but may also contribute to lifetime lung function impairment.

Multi-trigger wheeze in young children has been linked to increased risk of asthma and chronic respiratory diseases in later life [7]. Recurrent viral infection is a common trigger of wheezing in young children, especially in those aged <5 years. In addition, many children wheeze in response to allergic and nonallergic airborne triggers such as tobacco smoke, traffic-related and combustion-related air pollution, animal hair and dander, pollen and mould (fungal) spores, or other pollutant exposures [7, 8]. These
exposures in early life may be related to asthma and lung function through the vulnerable developing immune and respiratory systems. Firstly, infants’ immune responses of antigen presentation, phagocytosis and cytotoxicity are not totally understood; however, it is well known that the risk of asthma is enhanced if immune regulation is influenced by certain exposures in very early childhood [9]. Secondly, in addition to their potential influence on the neonatal immune system, early-life exposures may also be detrimental for development of healthy lungs. Newborn lungs are quite immature, and alveoli, capillary networks and airways grow rapidly in number and size until the child is 2 years old. After the age of 2 years, the lung continues to grow into adolescence, mainly by growth in volume of existing structures.

Many early-life household air exposures have been linked to asthma development and lung function impairment, for example tobacco smoke, cooking/heating, mould/dampness, pets and cleaning products. Although these exposures may also be harmful for older children, adolescents and adults, early childhood is a particularly vulnerable period, especially for indoor exposures. Infants are more highly exposed to many important household risk factors than adults. They spend most of their time indoors [10] and have an increased respiratory rate, inhaling more particulate matter relative to their body size [11]. Additionally, they usually breathe air closer to the ground, where airborne exposures are higher [12].

The evidence regarding the associations between early-life household air exposures, childhood asthma and lung function has not been comprehensively presented in previous reviews, as many of them focus on both childhood and adult asthma and/or present a broad overview of the full spectrum of risk factors. Identifying asthma is not easy in young children, as wheeze, the traditional symptom of asthma, may be caused by early-life respiratory infection [13]. This wheeze resolves with resolution of the infection and is often not indicative of asthma. Additionally, most asthma symptoms improve or disappear with age, although it is not currently possible to determine which early wheeze will resolve and which children will go on to have persistent asthma. Given the difficulties in defining childhood asthma in epidemiological studies, this review used a broader definition in conjunction with wheeze to include more asthma-related articles. This review summarises the epidemiological and mechanistic evidence linking early-life household air exposures before 2 years to outcomes of childhood asthma/wheezeing and lung function impairment.

Critical period for lung growth and asthma development

Household air exposures that contain allergens may increase the risk of atopic sensitisation and lead to asthma through the development of airway inflammation, bronchial hyperresponsiveness and reversible airflow obstruction. Common household allergens include animal dander, mould and dust, and exposure to these in sensitive individuals can trigger an allergic-type immune response. Early-life exposures may also modulate the immune system and can increase the risk of asthma. For instance, tobacco smoke may influence the immune regulation of infants. There is clear evidence that tobacco smoke impairs type 1 T-helper cell (Th1)-type responses with a shift to Th2 immunity together with enhanced secretion of pro-inflammatory cytokines [14]. An immune response polarised to a Th2 type with increased pro-inflammatory interleukin (IL)-1β/IL-17 is a feature observed in childhood asthma [9].

Early-life environmental exposures may also substantially influence lung growth. Neonates’ lungs may be especially vulnerable when moving from limited environmental exposures while in utero to diverse environmental exposures during and after birth. There is mounting epidemiological evidence that factors in the early-life environment have a major influence on lung health and maximally attained lung function. An Australian birth cohort observed that parental smoking during early life increased the risk of asthma, lung function impairment and lung growth in their children by adolescence, at 12 and 18 years [15]. A birth cohort study in Dunedin, New Zealand, found that >25% of children had wheezing that persisted into adulthood, and that the risk factors in early life included allergies, tobacco smoke exposure and early-age-onset asthma. In this study, adolescents with persistent wheezing had lower lung function in comparison to nonasthmatic and nonsmoking peers [3]. Although a newborn’s lungs are able to function at the time of birth, the lungs are still quite immature, as the alveoli (the site of gas exchange) are not completely formed. Alveoli start to form after 36 weeks of gestation and grow rapidly in number and size until the child is 2 years old in order to enlarge the gas-exchange surface area [16]. The respiratory tree of bronchi and bronchioles is complete at birth and they increase in size (length and diameter) after this time. Capillary networks including those surrounding alveoli for gas exchange are also formed during the first 2 years of life. Simple lung growth then starts after 2 years, as single lung weight increases from 60 g to 750 g, and the remaining volume of air in the lungs after maximal expiration (functional lung residual capacity) increases from ~80 mL at birth to 3000 mL in early adulthood [16]. Lung growth is largely complete in late-adolescent girls; by contrast, adolescent boys continue to increase their lung volume well into their mid-20s [17]. Given these growth
patterns, early-life adverse exposures may impair the ability to attain maximal lung function at the end of adolescence and may also influence the rate of decline (accelerate decline) in later life.

**Common early-life household air exposures**

The adverse household factors that have been implicated in asthma pathogenesis and lung growth, particularly during infancy and early childhood, include environmental tobacco smoke, cooking/heating, mould, pet ownership and chemical pollutants.

**Tobacco smoke exposure**

There is irrefutable evidence that personal smoking has adverse effects on respiratory health, and the association between smoking and lung disease is universally acknowledged, even by the tobacco industry. However, evidence on the impact of passive smoke exposure, especially early-life exposure, is still an active area of research (table 1). *In utero* exposure to maternal tobacco smoking is associated with increased rates of asthma and wheezing in later life [30]. Nicotine has been shown to have detrimental effects on fetal lung development [16, 31]. Associations have been found between both pre- and post-natal exposure to maternal smoking and wheezing and asthma in children; however, the available studies have been unable to untangle distinct contributions of pre- and post-natal smoking [32].

A few epidemiological studies have investigated whether there is an effect on children’s lungs of post-natal exposure to maternal smoking regarding childhood asthma; however, they have provided inconsistent evidence. An Australian study observed 4276 children from birth to age 14 years. In this study, maternal smoking was assessed during pregnancy, 3–5 days post-partum, at 6 months and at 5 years. This study found that pregnancy smoking only (OR 1.98, 95% CI 1.25–3.33) and post-natal smoke exposure only (OR 1.53, 95% CI 1.10–2.13) increased risk of child-reported asthma symptoms at age 14 [24]. Another large cohort study in western Norway (n=3786) found that children exposed to only pre- or only post-natal tobacco smoke did not have a substantial risk of developing adult asthma (self-reported doctor’s diagnosis) and respiratory symptoms. However, children exposed to maternal smoking at both periods had significant risks of all respiratory outcomes [33].

| First author (year) [reference] | Exposure age | Outcome age | Results |
|--------------------------------|--------------|-------------|---------|
| Cunningham (1994) [18]         | Pre-natal only and current smoking | 8–12 years | Pre-natal smoking associated with reduced lung function; current smoking was not associated with reduced lung function |
| Wang (1994) [19]               | The first 5 years | 6–18 years | Reduced lung function |
| Gilliland (2003) [20]          | *In utero* to post-natal maternal smoking | 7–18 years | Reduced lung function |
| Rizzi (2004) [21]              | During pregnancy and current smoking | Mean age 16 years | Reduced lung function |
| Jedrychowski (2005) [22]       | Maternal smoking post-natally | 9 years | Reduced lung function |
| Magnusson (2005) [23]          | The 36th week of gestation | 14–28 years | Increased risk of wheezing and hay fever |
| Alati (2006) [24]              | Last trimester, 6 months and 5 years | 14 years | *In utero* smoking increased risk of asthma in girls, but post-natal smoking (only) did not increase the risk of asthma (no associations were seen in boys) |
| Phabhu (2010) [25]             | 11 weeks, 20 weeks and 32 weeks of gestation | 2 and 5 years | Maternal smoking throughout pregnancy associated with reduced lung function; children whose mothers smoked during the first trimester were at increased risk of asthma at age 2 years, but had normal lung function |
| Chen (2011) [26]               | *In utero* and ETS before 5 years | 12–14 years | *In utero* smoking associated with early-onset asthma; ETS before 5 years associated with late-onset asthma |
| Grabenhainrich (2014) [27]     | *In utero* smoking | 20 years | Increased risk of asthma |
| Dai (2017) [15]                | Early-life smoking (mean time: 4 days before birth) | 12 and 18 years | Reduced lung function, lung growth and increased risk of asthma seen in girls, not in boys |
| Thacher (2018) [28]            | *In utero* smoking, during fetal life, infancy, childhood, adolescence | 14–16 years | *In utero* smoking was associated with increased risk of asthma and rhinoconjunctivitis; tobacco smoking after birth was not associated with adolescent-onset asthma or rhinoconjunctivitis |
| Huang (2018) [29]              | ETS before 3 years | 8 years | Increased risk of asthma |

ETS: environmental tobacco smoke.
Impaired lung growth may explain the subsequent increased risk of incidence in asthma associated with early-life tobacco smoke exposure, as many studies found that FEV₁ was more affected by tobacco smoke exposure than FVC. Dai et al. [34] observed that FEV₁, mid-expiratory flow (MEF) and FEV₁/FVC seemed to be reduced more than FVC at 18 years when participants were exposed to early-life maternal smoking (mean exposure time 4 days post-partum). The Dutch population-based Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort suggested that persistent childhood passive smoking (measured at 3 months after birth, annually from 1 to 8 years and at 11 years) was associated with reduced FEV₁ growth per year from the age of 12 to 16 years, but the association was not seen for FVC. Reductions in these specific lung function parameters (FEV₁, MEF and FEV₁/FVC) are markers of airway obstruction, a classic feature of asthma. Lung function obstruction over time may become irreversible as a consequence of asthma progression [35].

Interestingly, more recent studies have investigated pre-conception smoking exposure on asthma risk for children. A large registry-based cohort recorded smoking habits of women in early pregnancy and followed-up smoking behaviour and asthma in their children and grandchildren. Maternal grandmother’s smoking, independent of mother’s smoking, was associated with increased risk of early persistent asthma in their grandchildren (at 0–3 and 4–6 years) [36, 37]. In this study, early persistent asthma was defined by purchase of at least two asthma medications before 3 years and at least two after 3 years. Another multigeneration analysis suggested that father’s smoking before conception increased risk of parent-reported asthma for children at 10 years. These findings support possible epigenetic transmission of risk from tobacco smoking exposures in previous generations [38].

**Air emissions during cooking/heating**

Exposure to tobacco smoke and lung health has been well studied. However, there is currently a lack of evidence concerning this relationship for cooking/heating emissions in household settings, although both tobacco smoke and solid fuel/biomass/gas may have similar effects, given they generate small-sized particulate matter (diameter <2.5 µm) (PM$_{2.5}$) that can reach smaller airways on inspiration. It is acknowledged that inhaled PM$_{2.5}$, due to daily cooking, may generate air pollution amounts equivalent to smoking one cigarette per day [39]. Combustion of solid fuel, an important contributor to indoor air pollution in developing countries, also releases various gases including nitrogen oxides, carbon monoxide and carbon dioxide, which are all associated with lung damage.

Exposure to cooking/heating smoke occurs throughout life, including critical periods of lung development, and it may even start in utero, continuing during childhood and adulthood. Several cross-sectional and longitudinal studies have found that exposure to solid-fuel smoke increases risk of asthma and poor lung growth in children and young adults [40–42]. However, the potential for severe impact of exposure during early life, especially during the critical period for lung growth, has not been adequately addressed [39]. There is currently limited evidence on early-life exposure to fuel smoke from cooking/heating and whether this is likely to lead to adverse respiratory outcomes in later life. For example, the PIAMA birth cohort investigated 3590 children from birth to 8 years and found that ever-exposure gas cooking was associated with prevalent asthma (parent-reported doctor’s diagnosis) only in girls (OR 1.97, 95% CI 1.05–3.72) [40]. A recent African study found that pre-natal and post-natal exposure to firewood/kerosene and ethanol led to poorer lung function, assessed using oscillometry in 2-year-old children [43].

Air filter devices could be an effective strategy for improving household air quality for homes that generate air emissions from cooking/heating. A recent study indicated that sericin-coated polyester based air filters can remove PM$_{2.5}$ and PM$_{10}$ from household fuel burning, reducing particulates from levels of 1000 µg·m$^{-3}$ to 5 µg·m$^{-3}$ within half an hour of operation [44]. Alternatively, effective house ventilation can also modify adverse respiratory health from cooking/heating exposure in children [45, 46]. However, there is a lack of evidence demonstrating whether any of these interventions can eliminate the impact of household air pollution during the critical window time for lung development in early life.

**Mould/dampness**

Mould and dampness have been reported to be related to higher risk of childhood asthma in several reviews [47, 48], although a few studies have not reported associations [49, 50]. Higher fungal allergen levels including Cladosporium spp., Alternaria spp., Aspergillus spp. and Penicillium spp. are found in houses with visible mould and signs of dampness [51, 52]. These diverse allergens are very small (usually 2–10 µm), allowing easy penetration and lodgement in the airways. They may bind antigen-specific immunoglobulin (Ig)E to mast cells or basophils that are associated with hypersensitivity or allergic reactions. Some fungal spores also release damaging mycotoxins that cause systemic inflammation, which can subsequently induce airway obstruction leading to symptoms of asthma [53]. A meta-analysis of eight
European birth cohorts reported a positive association between early exposure to visible mould and/or dampness during the first 2 years of life and the development of asthma in children aged between 3 and 10 years [54].

Few studies have followed-up participants long enough to assess associations beyond childhood into adolescence. The Barn/Child Allergy Milieu Stockholm Epidemiology (BAMSE) study investigated mould/dampness exposure for 4089 infants at 2 months of age and found increased risk of ISAAC questionnaire-defined asthma at 16 years of age [55]. In contrast, the Dutch PIAMA study (n=1871) found no evidence of an association between early-life mould/dampness and Mechanisms of the Development of Allergy (MeDALL) protocol-defined asthma at the age of 17 years. In the PIAMA study, exposure was measured over a longer period at 3 months and 6 months, and then annually until 8 years [49]. The reason for the inconsistency is unclear. Home dampness may lead to asthma causing exposures including growth of fungi and bacteria, and increased emissions from some chemical pollutants used to treat the mould [56]. Lack of quantitative measurements of total mould counts may also be a reason for inconsistent associations [57].

Early-life mould/dampness may be harmful for lung function growth in childhood. The PIAMA birth cohort suggested that early-life exposure to mould (or dampness) was associated with reduced lung function growth in FEV₁ and FVC between 12 and 16 years, but these associations were not found when exposure was during mid- or later childhood [58]. This study did not specify the mean time and range for early-life exposure.

Dogs and cats
Higher household allergens have clear asthma implications through the development of bronchial hyperresponsiveness and airway inflammation in sensitised subjects [59]. Given that homes with cats and dogs have elevated levels of allergens in both dust and air samples, including Canis familiaris 1 and Felis domesticus 1 [60–62], having pets at home is expected to have an impact on asthma. However, epidemiological studies have reported contradictory associations between early-life cat and dog exposure and asthma and lung function, depending on the study design and establishment of time sequence between exposure and disease. In general, birth cohorts have not found cat or dog exposure during early life to be associated with increased risk of childhood asthma or impaired lung function [63–66] (table 2). However,
early-life exposure may have effects on respiratory health that are different from the effects of exposures at other times, as it is an important window for respiratory system development. The PIAMA cohort found that early-life cat exposure was associated with reduced FVC growth in adolescence between 12 and 16 years, but there was no significant influence on MeDALL protocol-defined asthma at 17 years, while other timings of exposure during childhood had no impacts on asthma and lung function in adolescence. A cohort study of 7326 school-aged children in China found that pet exposure in the first 2 years of life was associated with reduced FVC. Adverse associations were more likely to be reported in cross-sectional studies or nonbirth cohorts. This inconsistency may be due to reverse causation, where people with asthma choose not to have pets, or recall bias among participants with current asthma. Ascertainment of pet ownership retrospectively is more likely to lead to recall bias and a positive association between pet keeping and increased risk of asthma. Longitudinal study designs can more accurately ascertain the direction of causality for the relationship between early-life cat and dog exposure and asthma. Other than study design, there may also be issues with the way cat and dog exposures are measured. This is often by questionnaires that make no direct measurement of the level or type of allergen exposure.

Interestingly, 60% of all wheezing symptoms before 6 years of age resolve by later childhood. The possible adverse outcomes for asthma development linked to pet exposure may also disappear over this time. The Lifestyle Immune System Allergy (LISA) birth cohort study suggested that cat allergens at 3 months were associated with early wheezing at 2 years, but these associations disappeared at 4 and 6 years. In the longer term, many studies show that early-life exposure is protective for asthma. A Swedish birth cohort showed that keeping a dog in the first year of life had an inverse association with late onset wheezing at 4 years; a UK population-based study also found that cat ownership during pregnancy was associated with reduced risk in offspring of persistent wheezing from 6 months to 7 years of age. One hypothesis is that limited exposure to cat or dog allergens may induce immune tolerance and reduce the risk of developing elevated IgE against other allergens during later life. However, the threshold of exposure that may induce harm is unclear.

Cleaning products

In the past decade, increasing evidence has suggested that exposure to cleaning products may cause airway irritation and chronic inflammation, subsequently leading to asthma symptoms and reduced lung function. A longitudinal prospective birth cohort of 3455 children in Canada observed increased risk of recurrent wheeze and physician-diagnosed asthma at 3 years in children living in homes with a higher frequency of use of cleaning products during infancy. This Canadian study raised concerns about irritative effects of cleaning products on the respiratory system during early life. In fact, the cleaning products may influence the risk even before birth. A recent study suggested that exposure starting around conception, pregnancy and birth was associated with questionnaire-defined asthma for offspring at 10 years, but exposure only starting after birth was not associated with asthma risk. Such airway irritants may pose hazards to developing airways for unborn babies through maternal transfer via the placenta. Studies looking at longer-term outcomes associated with cleaning product exposure after school age are required to explore possible long-term associations.

Understanding cleaning product ingredients is important to precisely explain the mechanisms of risk. Many fragrant cleaning products contain volatile organic compounds (VOCs). Some VOCs have been linked to asthma, atopic dermatitis and allergies. Other common active ingredients in disinfectants include quaternary ammonium compounds and sodium hypochlorite, which have also been linked to reduced airway function. Spray products such as air fresheners may be particularly hazardous, because they facilitate aerosolised exposure. Secondary exposures may be created when VOCs are mixed with other household air pollution. Understanding cleaning product ingredients is important to precisely explain the mechanisms of risk. Many fragrant cleaning products contain volatile organic compounds (VOCs). Some VOCs have been linked to asthma, atopic dermatitis and allergies. Other common active ingredients in disinfectants include quaternary ammonium compounds and sodium hypochlorite, which have also been linked to reduced airway function. Spray products such as air fresheners may be particularly hazardous, because they facilitate aerosolised exposure. Secondary exposures may be created when VOCs are mixed with other household air pollution, but the influence of secondary exposure is still not fully understood.

Implications and recommendations

Establishing an asthma-friendly home environment for infants and young children

Early-life exposures including tobacco smoke, mould and cleaning products are associated with long-term risks of asthma and lung function deficits. This evidence has the potential to be translated into important public messages to avoid or minimise household air exposures that lead to adverse respiratory health. Clinicians could advise parents of infants and young children to modify their homes to ensure an asthma-friendly home environment, when assessing children with early wheeze or asthma and developing management plans. Asthma-friendly home environments are those that endeavour to keep the indoor air as clean as possible. A key component of an asthma-friendly home environment is that it is smoke-free. Indoor air should be free of tobacco smoke, which contains irritants and chemicals known to be harmful for respiratory health. Public health messages should continue to advocate for protection from tobacco smoke exposure for pregnant women and infants.
Energy source selection at home is also linked to risk of childhood asthma and lung function deficits. Combustion of gas and wood generates a complex mixture of carbon-based particles and gases that may have health effects in children. Electric technologies can reduce the release of particulates from combustion activities in the home. It is particularly important to ventilate houses when using home heating and cooking systems that can generate high levels of pollutants, such as gas cooking and solid fuel combustion.

Based on this review, there is little evidence that early-life exposure to cats or dogs has an impact on the development of asthma and lung function impairment. The evidence is currently inconsistent, and no recommendations can be made.

**Using cleaning products safely for young children**

Although the link between cleaning products and respiratory health is suggestive, cleaning products are still extremely popular, particularly during flu season and during the coronavirus disease 2019 pandemic. To avoid the risks, it may be important to reduce the frequency of cleaning product use and select less harmful products. However, a lack of information and product labelling means that consumers are often not aware of potentially harmful chemicals present in these products [88]. Unfortunately, current disclosure regulations have led to a lack of transparency on cleaning products.

However, given the accumulating evidence, the American Lung Association recommends using cleaning products that “don’t have VOCs, fragrances, irritants or flammable ingredients” [91]. Many strategies may be applied to minimise exposure for infants and young children; parents may avoid using cleaning products around children, allow adequate ventilation during and after cleaning activities, use dilute concentrations, avoid using multiple products together and rinse surfaces with water following product use [90].

**Conclusions**

In conclusion, many early-life household exposures in terms of tobacco smoke, mould and cleaning products are associated with childhood asthma development and reduced lung function growth. This literature review supports the hypothesis that asthma and lung function development and decline are programmed early in life and advances our understanding of timing of exposure on respiratory health. The household environment during early life is of critical importance in ensuring healthy lung development, and it may be important to develop preventive strategies for infants to avoid potentially adverse exposures and maximise their future respiratory health.

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**References**

1. Mallol J, Crane J, von Mutius E, et al. The International Study of Asthma and Allergies in Childhood (ISAAC) phase three: a global synthesis. *Allergol Immunopathol* 2013; 41: 73–85.
2. Global Asthma Network. The Global Asthma Report 2014. 2014. Available from: www.globalasthmareport.org/.
3. Sears MR, Greene JM, Willan AR, et al. A longitudinal, population-based, cohort study of childhood asthma followed to adulthood. *N Engl J Med* 2003; 349: 1414–1422.
4. London SJ, James Gauderman W, Avol E, et al. Family history and the risk of early-onset persistent, early-onset transient, and late-onset asthma. *Epidemiology* 2001; 12: 577–583.
5. Bui DS, Lodge CJ, Burgess JA, et al. Childhood predictors of lung function trajectories and future COPD risk: a prospective cohort study from the first to the sixth decade of life. *Lancet Respir Med* 2018; 6: 535–544.
6. Saglani S, Payne DN, Zhu J, et al. Early detection of airway wall remodeling and eosinophilic inflammation in preschool wheezers. *Am J Respir Crit Care Med* 2007; 176: 858–864.
7. Brand PL, Balardi E, Bisgaard H, et al. Definition, assessment and treatment of wheezing disorders in preschool children: an evidence-based approach. *Eur Respir J* 2008; 32: 1096–1110.
Duelien T, Eagan TML, Eide GE, Silvestri M, Franchi S, Pistorio A, Burri PH. Structural aspects of postnatal lung development.

Tager IB. The effects of second-hand and direct exposure to tobacco smoke on asthma and lung function in children. Pediatrics 2004; 113: 996–1006.

Parks J, Takaro TK. Exposure to cleaning products and childhood asthma: more than just a link? Expert Rev Respir Med 2020; 14: 1185–1188.

Ladruption KC, Pijnenburg MW. Monitoring asthma in childhood. Eur Respir Rev 2015; 24: 178–186.

Strzelak A, Ratajczak A, Adamiec A, et al. Tobacco smoke induces and alters immune responses in the lung triggering inflammation, allergy, asthma and other lung diseases: a mechanistic review. Int J Environ Res Public Health 2018; 15: 1033.

Dai X, Dharmage SC, Lowe AJ, et al. Early smoke exposure is associated with asthma and lung function deficits in adolescents. J Asthma 2017; 54: 662–669.

Merkus PJ, ten Have-Otbroek AA, Quanjer PH. Human lung growth: a review. Thorax 1999; 54: 1119–1138.

Becklake MR, Kauffmann F. Gender differences in airway behaviour over the human life span. Thorax 1999; 54: 1119–1138.

Cunningham J, Dockery DW, Speizer FE. Maternal smoking during pregnancy as a predictor of lung function in children. Am J Epidemiol 1994; 139: 1139–1152.

Wang XB, Wypij D, Gold DR, et al. A longitudinal study of the effects of parental smoking on pulmonary function in children 6–18 years. Am J Respir Crit Care Med 1994; 149: 1420–1425.

Gilliland FD, Berhane K, Li Y-F, et al. Effects of early onset asthma and in utero exposure to maternal smoking on childhood lung function. Am J Respir Crit Care Med 2003; 167: 917–924.

Rizzi M, Sergi M, Andreoli A, et al. Environmental tobacco smoke may induce early lung damage in healthy male adolescents. Chest 2004; 125: 1387–1393.

Jedrychowski W, Mauger U, Jedrychowska-Bianchi I, et al. Effect of indoor air quality in the postnatal period on lung function in pre-adolescent children: a retrospective cohort study in Poland. Public Health 2005; 119: 535–541.

Magnarsson LL, Olesen AB, Wennborg H, et al. Wheezing, asthma, hayfever, and atopic eczema in childhood following exposure to tobacco smoke in fetal life. Clin Exp Allergy 2005; 35: 1550–1556.

Alati R, Al Mamun A, O’Callaghan M, et al. In utero and postnatal maternal smoking and asthma in adolescence. Epidemiology. 2006; 17: 138–144.

Prabhu N, Smith N, Campbell D, et al. First trimester maternal tobacco smoking habits and fetal growth. Thorax 2010; 65: 235–240.

Chen Y-C, Tsai C-H, Lee YL. Early-life indoor environmental exposures increase the risk of childhood asthma. Int J Hyg Environ Health 2011; 215: 19–25.

Grabhenrich LB, Gough H, Reich A, et al. Early-life determinants of asthma from birth to age 20 years: a German birth cohort study. J Allergy Clin Immunol 2014; 133: 979–988.

Thacher JD, Gehring U, Gruzieva O, et al. Maternal smoking during pregnancy and early childhood and development of asthma and rhinoconjunctivitis – a MeDALL project. Environ Health Perspect 2018; 126: 047005.

Huang C-C, Chiang T-L, Chen P-C, et al. Risk factors for asthma occurrence in children with early-onset atopic dermatitis: an 8-year follow-up study. Pediatr Allergy Immunol 2018; 29: 159–165.

Tager IB. The effects of second-hand and direct exposure to tobacco smoke on asthma and lung function in adolescence. Paediatr Respir Rev 2008; 9: 29–38.

Burrin PH. Structural aspects of postnatal lung development – alveolar formation and growth. Biol Neonate 2006; 89: 313–322.

Silvestri M, Franchi S, Pistorio A, et al. Smoke exposure, wheezing, and asthma development: a systematic review and meta-analysis in unselected birth cohorts. Pediatr Pulmonol 2015; 50: 353–362.

Duelien T, Eagan TML, Edie GE, et al. The adult incidence of asthma and respiratory symptoms by passive smoking in utero or in childhood. Eur Respir Rev 2006; 15: 226–227.

Dai X, Dharmage SC, Bowatte G, et al. Interaction of glutathione S-transferase M1, T1, and P1 genes with early life tobacco smoke exposure on lung function in adolescents. Chest 2019; 155: 94–102.

Pascal RM, Peters SP. The irreversible component of persistent asthma. J Allergy Clin Immunol 2009; 124: 883–890.

Bräbäck L, Lodge CJ, Lowe AJ, et al. Childhood asthma and smoking exposures before conception – a three-generational cohort study. Pediatr Allergy Immunol 2018; 29: 361–368.

Lodge CJ, Bräbäck L, Lowe AJ, et al. Grandmaternal smoking increases asthma risk in grandchildren: a nationwide Swedish cohort. Clin Exp Allergy 2018; 48: 167–174.
66 Chen CM, Morgenstern V, Bischof W, et al. Dog ownership and contact during childhood and later allergy development. *Eur Respir J* 2008; 31: 963–973.

67 Remes ST, Castro-Rodriguez JA, Holberg CJ, et al. Dog exposure in infancy decreases the subsequent risk of frequent wheeze but not of atopy. *J Allergy Clin Immunol* 2001; 108: 509–515.

68 Heissenhuber A, Heinrich J, Fahlbusch B, et al. Health impacts of second-hand exposure to cat allergen Fel d 1 in infants. *Allergy* 2003; 58: 154–157.

69 Sandin A, Björkstén B, Bräbäck L, et al. Development of atopy and wheezing symptoms in relation to herdity and early pet keeping in a Swedish birth cohort. *Pediatr Allergy Immunol* 2004; 15: 316–322.

70 Hagendorens MM, Bridts CH, Lauwers K, et al. Perinatal risk factors for sensitization, atopic dermatitis and wheezing during the first year of life (PIPO study). *Clin Exp Allergy* 2005; 35: 733–740.

71 Campo P, Kalra HK, Levin L, et al. Influence of dog ownership and high endotoxin on wheezing and atopy during infancy. *J Allergy Clin Immunol* 2006; 118: 1271–1278.

72 Pohlabeln H, Jacobs S, Böhmann J. Exposure to pets and the risk of allergic symptoms during the first 2 years of life. *J Investig Allergol Clin Immunol* 2007; 17: 302–308.

73 Herr M, Just J, Nikasínovic L, et al. Influence of host and environmental factors on wheezing severity in infants: findings from the PARIS birth cohort. *Clin Exp Allergy* 2012; 42: 275–283.

74 Gaffin JM, Spergel JM, Boguniewicz M, et al. Effect of cat and daycare exposures on the risk of asthma in children with atopic dermatitis. *Allergy Asthma Proc* 2012; 33: 282–288.

75 Collin SM, Granell R, Westgarth C, et al. Associations of pet ownership with wheezing and lung function in childhood: findings from a UK birth cohort. *PLoS One* 2015; 10: e0127756.

76 Hu LW, Qian Z, Dharmage SC, et al. Pre-natal and post-natal exposure to pet ownership and lung function in children: the Seven Northeastern Cities Study. *Indoor Air* 2017; 27: 1177–1189.

77 Salo PM, Xia J, Anderson Johnson C, et al. Indoor allergens, asthma, and asthma-related symptoms among adolescents in Wuhan, China. *Ann Epidemiol* 2004; 14: 543–550.

78 Martínez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. *N Engl J Med* 1995; 332: 133–138.

79 Chen C-M, Rzehak P, Zutavern A, et al. Longitudinal study on cat allergen exposure and the development of allergy in young children. *J Allergy Clin Immunol* 2007; 119: 1148–1155.

80 Chen C-M, Tischer C, Schnappinger M, et al. The role of cats and dogs in asthma and allergy – a systematic review. *Int J Hyg Environ Health* 2010; 213: 1–31.

81 Sherriff A, Farrow A, Golding J, et al. Frequent use of chemical household products is associated with persistent wheezing in pre-school age children. *Thorax* 2005; 60: 45–49.

82 Choi H, Schmidbauer N, Sundell J, et al. Common household chemicals and the allergy risks in pre-school age children. *PLoS One* 2010; 5: e13423.

83 Siracus aA, Blay F, Folletti I, et al. Asthma and exposure to cleaning products – a European Academy of Allergy and Clinical Immunology task force consensus statement. *Allergy* 2013; 68: 1532–1545.

84 Casas L, Zock J-P, Torrent M, et al. Use of household cleaning products, exhaled nitric oxide and lung function in children. *Eur Respir J* 2013; 42: 1415–1418.

85 Henderson J, Sherriff A, Farrow A, et al. Household chemicals, persistent wheezing and lung function: effect modification by atopy? *Eur Respir J* 2008; 31: 547–554.

86 Parks J, McCandless L, Dharm aC, et al. Association of use of cleaning products with respiratory health in a Canadian birth cohort. *CMAJ* 2020; 192: E154–E161.

87 Tjalvin G, Svanes Ø, Igland J, et al. Maternal preconception occupational exposure to cleaning products and disinfectants and offspring asthma. *J Allergy Clin Immunol* 2022; 149: 422–431.

88 Steinemann AC, MacGregor IC, Gordon SM, et al. Fragranced consumer products: chemicals emitted, ingredients unlisted. *Environ Impact Assess Rev* 2011; 31: 328–333.

89 Clausen PA, Frederiksen M, Sejbæk CS, et al. Chemicals inhaled from spray cleaning and disinfection products and their respiratory effects. A comprehensive review. *Int J Hyg Environ Health* 2020; 229: 113592.

90 Singer BC, Coleman BK, Destaillats H, et al. Indoor secondary pollutants from cleaning product and air freshener use in the presence of ozone. *Atmos Environ* 2006; 40: 6696–6710.

91 American Lung Association. Cleaning Supplies and Indoor Chemicals. 2020. www.lung.org/clean-air/at-home/indoor-air-pollutants/cleaning-supplies-household-chem Date last accessed: 15 December 2021. Date last updated: 13 July 2020.

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