Published in final edited form as:
*Curr Allergy Asthma Rep*. 2011 October ; 11(5): 414–420. doi:10.1007/s11882-011-0206-7.

# Impact of Environmental Controls on Childhood Asthma

**Devika Rao**
Division of Respiratory Diseases, Children's Hospital Boston, 300 Longwood Avenue, Mailstop 208, Boston, MA 02215, USA devika.rao@childrens.harvard.edu

**Wanda Phipatanakul**
Division of Immunology, Children's Hospital Boston, Fegan 6, 300 Longwood Avenue, Boston, MA 02115, USA wanda.phipatanakul@childrens.harvard.edu

## Abstract

Exposure to allergens early in life can lead to sensitization and the development of childhood asthma. It is thought that increased exposure with the advent of modern housing is likely contributing to the rise in prevalence of childhood asthma during the past few decades. The progression from allergen exposure to sensitization and asthma development has been noted with respect to dust mites, pets, cockroach, mouse, mold, tobacco smoke, endotoxin, and air pollution, although some have found a protective effect with pet and endotoxin exposure. Recent studies have shown that allergen remediation may be beneficial in reducing asthma morbidity and development, although there is also some evidence to the contrary. Examples of allergen remediation that have been studied include the use of dust mite–impermeable covers, high-efficiency particulate air filtration, integrated pest management, home repairs, ventilation improvement, and pet removal. Several multifaceted, randomized controlled trials have shown that reducing multiple early allergen exposures with environmental controls is associated with a decreased risk of asthma.

### Keywords

Asthma; Asthma prevention; Asthma control; Children; Allergen; House dust mites; Home remediation; Mold; Endotoxin; Integrated pest management; Pollution; Cats; Dogs; Tobacco

## Introduction

It has been speculated that the reason for the increase in childhood asthma over the past few decades is a change in environmental exposures. The advent of modern housing has led to higher indoor temperatures and increased humidity, and combined with an increase in furnishings, the home environment is very vulnerable to high levels of allergens such as dust mites and molds. Furthermore, evidence indicates that sensitization to indoor allergens (eg, house dust mite [HDM]) rather than outdoor allergens (eg, grass pollen) is a stronger risk factor for the development of asthma [1, 2].

Allergic childhood asthma is thought to begin first with exposure to an inciting allergen, followed by sensitization and the development of asthma or atopy. The timing of the exposure may be important. Exposure beginning in infancy has been shown to place infants with a family history of atopy at higher risk of the development of allergic diseases,

**Disclosure** Dr. Phipatanakul has served on boards for the New England Society of Allergy and MedImmune and has received grant support from AstraZeneca.
Dr. Rao reported no potential conflicts of interest relevant to this article.

including asthma [1, 3]. Given that childhood asthma may begin with an early exposure, the utility of preventive measures to reduce allergen exposure has been studied. Specifically, attention has been given to altering the home environment with remediation techniques to reduce exposures. The purpose of this review is to discuss the common allergens found in homes and schools that are associated with sensitization and with childhood asthma. We also discuss the recent evidence that examines the efficacy of environmental controls in reducing childhood asthma morbidity.

## Dust Mite

The relationship among HDM exposure, sensitization, and childhood asthma has been well-studied. It has been shown that there is a dose–response relationship between HDM allergen and sensitization [4], and that sensitization is associated with increased risk of asthma-related hospitalizations, unscheduled visits, and medication use [5]. The risk of developing asthma was particularly increased in high-risk infants with early exposure to high levels of HDM allergen (≥10 μg/g) [6]. The use of mite-impermeable covers as a control measure is debated. A prospective, double-blind, placebo-controlled study involving 60 children randomly assigned to receive mattress and pillow covers or sham covers found a reduction in HDM allergen in the treatment group compared with the control group. Furthermore, this reduction in allergen levels appeared to translate to significantly lowered doses of inhaled corticosteroids (ICS) in the 1-year follow-up period [7]. However, a more recent study of 143 HDM-allergic asthmatics requiring ICS (16–60 years of age) showed that HDM-impermeable mattress and pillow covers did not improve ICS use compared with sham encasings, which may be explained by relatively low levels of HDM allergens and good asthma control at baseline [8]. Another double-blind, randomized, placebo-controlled study analyzing the effectiveness of allergen-impermeable bed covers in 1,122 asthmatic adults also did not show any benefit [9]. Results from the Isle of Wight birth cohort also demonstrated a decreased risk of asthma at 8 years of age in the intervention group, although HDM avoidance was part of a multifaceted intervention, and it was difficult to determine which intervention led to the decreased risk [10].

Feather-based bedding has been associated with lower levels of HDM allergen compared with synthetic bedding [11, 12]. A recent randomized controlled trial studied 197 HDM-sensitized moderate to severe asthmatic children to examine the difference between feather bedding and HDM bedding covers. In this study, both the treatment and control groups received dust mite covers, while the treatment group additionally received feather bedding. The authors reported no significant differences between the two groups in terms of wheezing episodes or quality of life, which may be explained in part by poor compliance with the use of feather bedding in the treatment group and some feather bedding use in the control group. However, a compliance analysis (rather than intention-to-treat analysis) revealed a possible association between feather bedding and improved respiratory symptoms, although recall bias may have influenced the results [13].

In another study using the Tasmanian infant cohort, Trevillian et al. [14] examined the utility of a more comprehensive environmental approach to analyzing the relationship between HDM control and asthma, hypothesizing that the levels of HDM allergen are influenced by a combination of bedroom environmental factors. The authors showed a significant increased risk of recent wheeze and childhood asthma at age 7 years in those families using two or more synthetic infant bedding items (adjusted OR, 2.10). This association was further strengthened by the use of heating, recent bedroom painting, and use of bedroom carpeting. The risk was increased fivefold in the case of the association between recent painting and risk of wheeze by age 7. Other measures in controlling HDM levels, which to our knowledge have not been recently re-examined in intervention studies, include

weekly washing of bedding with heated drying; avoidance of carpeting, upholstered furniture, and stuffed animals; and keeping humidity levels below 50% [15]. However, a recent meta-analysis of 54 trials from 1966 to 2007 involving HDM-allergic asthmatics showed that interventions including acaricides, mattress covers, vacuum cleaning, washing, air filtration, and ionizers were not successful in reducing HDM levels or asthma symptom scores compared with placebo or no treatment [16]. Despite the results of these studies, many factors, such as sample size, multiple other sensitizations, and exposures, may account for the results in these HDM studies, and in general, standard-of-care practitioners routinely recommend dust mite control measures for patients who are dust mite allergic.

## Pets

Some evidence indicates that early exposure to pets is associated with decreased sensitization to common aeroallergens in atopic and nonatopic children [17], although this also has been debated. Early dog exposure may have a protective effect for childhood asthma, especially in those without an atopic family history. Similarly, exposure to high levels of cat allergen has been shown to be associated with decreased sensitization [18] and may be protective for asthma [19]. However, a meta-analysis showed that early pet exposure is associated with an increased risk of asthma [20].

A recent study utilizing the Prevention and Incidence of Asthma and Mite Allergy (PIAMA) birth cohort analyzed the association between cat or dog exposure yearly up to age 8 years and allergen sensitization, along with asthma development [21•]. The authors reported that dog exposure at 3 months was associated with a decreased risk of sensitization to any allergen (OR, 0.49; $P<0.01$), while cat exposure at 3 months was associated with a decreased risk of HDM sensitization (OR, 0.68; $P=0.02$). Although these findings call into question any protective effect pet exposure may have, the PIAMA study did not find a significant association between early pet exposure and asthma development at age 8 years. Therefore, it is unclear based on conflicting evidence whether elimination of pet prevents childhood asthma development. Studies analyzing the effect of pet removal on asthma are few, although Shirai et al. [22] reported a reduced need for ICS in pet-allergic asthmatics who removed the pet from the home. The current standard of care is to recommend pet removal in those patients who have a proven pet allergy.

## Cockroach/Pest Management

High levels of cockroach allergen and mouse allergen have been well-described in the homes of urban children, although there appear to be regional differences. A total of 98% of 101 kitchen dust samples from 101 apartments in Gary, IN, had detectable levels of Bla g 1 allergen [23], while a study examining samples from inner-city Baltimore schools found cockroach allergen in 66% of dust samples [24]. A multicenter intervention study by Morgan et al. [25] reported 68.4% of sampled bedrooms had detectable cockroach allergen levels. Chew et al. [26] recently noted that exposure to cockroach allergen was associated with sensitization in a dose–response manner in a group of inner-city children, while results from the National Cooperative Inner City Asthma Study indicate that asthmatic children sensitized to cockroach have an almost twofold higher risk of asthma-related hospitalizations [5]. Data from the National Cooperative Inner City Asthma Study also showed that the combination of cockroach allergy and exposure to high levels of allergen was associated with higher rates of missed school days, wheezing, and hospitalizations [27].

Like cockroach allergen, mouse allergen exposure is associated with a high rate of mouse sensitization [28]. Mouse allergen has also been shown to be a significant exposure among school-aged children in schools and in homes [29, 30•], although the school exposure may be more significant. In a study of four inner-city Boston schools, Sheehan et al. [30•]

reported that asthmatic students attending the school with the highest levels of mouse urinary protein also had more reported missed school days due to asthma. Thus, it is imperative to consider potential exposures that asthmatic children may have outside the home as targets for allergen control.

Integrated pest management (IPM) has been shown to be an effective control in reducing cockroach and allergen levels, although to our knowledge, all studies have focused on IPM measures in the home. IPM involves a combination of tactics aimed at pest elimination with the use of pesticides and baits but also involves a long-term plan to prevent reinfestation by improving structural conditions in the home via crack sealing, hole repair, and pest food source removal. IPM has been shown to reduce levels of cockroach allergen, although a study by Peters et al. [31] showed that allergen levels began to increase 6 months after the intervention. A study by Kass et al. [32] used IPM at the building level rather than at the level of individual apartments in New York City public housing. The authors compared IPM intervention in eight buildings with five buildings that employed traditional pest control measures. They reported that bedroom Bla g 2 levels 6 months after IPM were 40% lower in the intervention group compared with the control group, and 30% lower compared with controls in the kitchen at 6 months [32]. The results also appeared to translate to 57% lower weekly cockroach counts at 3-month follow-up in the IPM group compared with the control group, although this difference was not significantly sustained at 6 months.

Kass et al. [32] did not report improvements in mouse sightings or mouse allergen with IPM, although this was likely due to the overall reduced amounts of mouse infestation in the New York area. However, Phipatanakul et al. [33] showed that an intervention in Boston (a city with more reported mouse allergen exposure) that included sealing holes, vacuuming, and using low-toxicity pesticides and traps resulted in reduced mouse allergen levels. The Inner-City Asthma Study was a randomized controlled trial of an intervention that targeted cockroaches and rodents, although the intervention was based on influencing behavior change rather than using IPM or pest control; the investigators reported a reduction in Bla g 1 even at the 2-year follow-up, and also found a strong correlation between cockroach allergen reduction and decreased asthma morbidity [25]. Based on these studies, it appears that IPM is effective in controlling cockroach and mouse infestation, but the results may be difficult to sustain. More longitudinal studies are needed to examine not only the effectiveness of pest control, but also whether IPM can result in decreased childhood asthma morbidity. Our group is currently studying mouse-allergic children and whether IPM may decrease asthma morbidity. Examining the effects of IPM in inner-city schools is also an important area of future study.

## Mold

The specific molds that have been implicated in asthma include *Alternaria alternata*, *Cladosporium* spp, *Aspergillus* spp, and *Penicillium* spp [34], although *Alternaria* is relatively better studied. Sensitization to *Alternaria* has been associated with an increased risk of hospitalization among inner-city asthmatic children [5]. A recent meta-analysis of 33 studies found that building dampness and mold were associated with respiratory symptoms and even asthma in children and adults, with ORs ranging from 1.37 to 1.75 [35], while another meta-analysis cited a strong association between mold exposure and childhood asthma exacerbations [36]. Results from the Cincinnati Childhood Allergy and Air Pollution Study found that children in their birth cohort with verified high levels of home mold exposure had a sevenfold greater risk of asthma as measured by the Asthma Predictive Index [37]. Another longitudinal birth cohort study of 396 children similarly described an association between both moisture damage and visible mold by 18 months of age [38].

Mold remediation and its effect on childhood asthma has not been as well-studied compared with HDM allergen, although both the school and home environments have been targeted for mold control measures. In their analysis of mold levels in Finland, Lignell et al. [39] reported that levels decreased in an elementary school with poor indoor air quality after a thorough renovation. The renovation included installation of an exhaust system and an air ventilation system [39]. The authors, however, were unable to demonstrate a significant difference in respiratory symptom complaints. Kercsmar et al. [40] examined the effects of a home-based mold remediation on 62 asthmatic inner-city children with home mold exposure. The intervention group, like in the Lignell et al. [39] study, had extensive repairs made in the home aimed at reducing mold exposure, such as leak repair, ventilation alteration, removal of water-damaged materials, and improvements in damp basements. They reported a significant reduction in mold scores at the 1-year follow-up, along with a reduction in emergency department visits and hospitalizations, in the remediation group [40]. These studies provide some evidence that mold levels can be controlled, although achieving this control in both studies required expensive renovations that may not be generalizable, especially in poorer urban communities. This may be the reason why control measures for mold were not readily adopted by families of childhood asthmatics enrolled in a study by Parker et al. [41]. One of the findings of this study was that these families, despite having have nine visits by a “community environmental specialist” over a period of 1 year, were less inclined to adopt behaviors to control mold exposure. Nevertheless, it is possible that comprehensive control measures may prove to be cost-effective measures in future studies and can help to decrease childhood asthma morbidity.

## Environmental Tobacco Smoke

It is well-known that exposure to environmental tobacco smoke (ETS) is associated with wheezing and increased asthma exacerbations in children. A total of 60% of children 3 to 11 years of age, or 22 million children, in the United States are exposed to ETS [42]. The risk of asthma and wheezing may be highest among teenagers who smoke and are also exposed to second-hand smoke [43].

The use of anticipatory guidance to reduce exposure to second-hand smoke has been shown to not significantly improve asthma symptoms; furthermore, a recent Cochrane review highlighted the ineffectiveness of most intervention studies whose aim was to reduce ETS exposure in children [44]. Given that it may not be plausible for some children to avoid ETS, the use of air filtration has been examined to help reduce asthma morbidity related to ETS. A recent study by Lanphear et al. [45] provided some evidence for use the use of high-efficiency particulate air (HEPA) air cleaners to reduce tobacco smoke exposure. These cleaners, which have been shown to reduce levels of airborne particles 0.3 μm or greater in size and nicotine, were used in a double-blind, randomized trial examining their effect on unscheduled asthma visits in a group of asthmatic children. The authors randomly assigned 100 children known to have cigarette smoke exposure to an intervention group and provided them with 2 HEPA filters for home use, while 115 children in the control group received a placebo (inactive) air cleaner. After adjusting for baseline difference, the authors found fewer unscheduled asthma visits in a 12-month follow-up period in the intervention group compared with the control group (185 vs 227; $P$=0.043), corresponding to an 18.5% reduction in the number of visits. The authors attributed this difference to a significant reduction in the number of airborne particles seen in the intervention group compared with the control group; however, there was no difference between the two groups with respect to serum or hair cotinine levels or air nicotine levels.

The best preventive control measure for ETS is to avoid exposure in the home. A recent study of 290 asthmatic children requiring daily controller therapy found that parental report

of decreased exposure to ETS over a 12-month period following enrollment was associated with decreased hospitalizations and emergency department visits [46]. These children also had less risk for an episode of poor asthma control (OR, 0.45; *P*=0.042) compared with children who had stable or increased exposure to ETS. A problem with this and other studies that use parental reports of smoking behavior is recall bias, which likely leads to overestimation of the intervention. Several multifaceted intervention trials also incorporate tobacco cessation in their methods [25, 47]. The Canadian Primary Prevention Study, which involved counseling of parents to cease smoking, did report lower second-hand smoke exposure in children in the intervention group, while the Inner-City Asthma Study reported no change in ETS exposure in their intervention group. Another randomized controlled trial that involved repeated visits by a community health worker with the goal of modifying parental behavior, including smoking habits, found no difference in the number of families reducing ETS in the home [41]. Regardless, clinicians should encourage parents to quit smoking given good evidence that associates secondhand smoke exposure with asthma morbidity in children.

## Endotoxin

Endotoxin is a component of the cell wall of gram-negative bacteria that is a potent stimulator of the immune system, and while inhaled endotoxin can cause bronchoconstriction and increased airway inflammation in adults, it is thought that early-childhood exposure may have a protective effect. Many have reported on the protective nature of endotoxin exposure in terms of its effect on childhood asthma development [48]; however, this is disputed by others. In a prospective birth cohort study of 440 children, Celedon et al. [6] found that early endotoxin exposure was associated with a reduced risk of atopy, but they also found an increased risk of wheezing at age 7 years in children with a family history of atopy. Another study found no association between endotoxin exposure in terms of risk of asthma or sensitization in children [49•]. If endotoxin exposure does influence asthma development, there may be simple ways to identify elevated levels in the home, making endotoxin exposure amenable to remediation studies. A recent study based in an urban area showed that certain home characteristics, including dampness and visible water damage, were associated with an increase in endotoxin levels, while once-weekly bedroom cleaning was associated with reduced levels [50].

## Air Pollution

Exposure to air pollutants has been associated with increased coughing, wheezing, and even asthma in the first 2 years of life [51], although there is debate as to whether exposure to traffic-related pollution can influence sensitization [52]. A more recent longitudinal analysis of a birth cohort associated with PIAMA showed that traffic pollution was associated with asthma and asthma-related symptoms at all ages up to 8 years of age [53]. Unfortunately, parents are likely contributing to increased exposure to pollution in light of a recent survey that reported that 75.0% of caregivers idle their vehicles within their community [54]). To our knowledge, no studies regarding diminished levels of air pollution and its effect on childhood asthma have been published, and this certainly would be a difficult but necessary area of study.

## Multifaceted Intervention Programs

A few studies have examined the effectiveness of a multifaceted intervention program on the primary prevention of asthma in high-risk infants, defined in these studies as unborn children with two or more atopic family members. Most children are sensitized to more than one allergen [1], and an environmental control approach that targets multiple allergens may be a necessary strategy. The Inner-City Asthma Study was a multicenter, randomized

controlled trial that tailored a customized intervention targeting skin test–positive allergens specific to asthmatic children 5 to 11 years of age. The investigators reported a decrease in asthma symptoms in the intervention group compared with the control group—a decrease that correlated with a significant decrease in dust and cockroach [25].

Targeting potential exposures of pregnant mothers with high-risk children also may be necessary given that sensitization may occur in utero. Miller et al. [55] found evidence of cord blood mononuclear cell proliferation in infants whose mothers had high home exposure to cockroach and mouse [55]. However, this finding was challenged by a more recent study that found that cord blood mononuclear cell proliferation was not associated with later sensitization as measured by allergen-specific IgE at ages 2, 3, and 5 years, and also was not associated with asthma at age 5 years [56].

Although there is conflicting evidence regarding in utero sensitization, several longitudinal, multifaceted, randomized controlled trials described the results of beginning the intervention before birth. The Canadian Primary Prevention Study (CPPS), begun in 1995, recruited pregnant mothers whose unborn children had a high asthma risk. A total of 279 of the infants' families underwent multifaceted intervention measures (avoidance of HDM, pets, and tobacco smoke; encouraging breastfeeding; and delayed introduction of solid foods), while 266 were assigned to a control group. The researchers found a decreased risk of asthma in nonatopic children in the intervention group, with an OR of 0.26 [57]. However, for those children who were atopic by 1 year of age and were persistently atopic at age 7, there was an increased asthma risk with an adjusted OR of 15.5. The authors did report, however, that the prevalence of asthma, defined as wheeze apart from colds along with bronchial hyperresponsiveness, was increased at 7 years of age in the intervention group [47]. Both Morgan et al. [25] and the CPPS lend support that multifaceted interventions aimed at controlling exposures in high-risk infants may help reduce asthma risk, but that atopic status at 1 year of age may be a strong predictor of the development of asthma despite control measures to reduce exposure.

The Isle of Wight prevention study also showed a decreased risk of childhood asthma at 8 years of age in those infants randomly assigned to the prophylactic group, which was characterized by HDM control with dust mite covers, acaricide, and food elimination diet in pregnant mothers (OR, 0.24; $P$=0.005) [10]. A strength of this study was the 100% follow-up rate at 8 years of age, although the intervention was not as comprehensive (no pet control, no avoidance of second-hand smoke) as the CPPS. There was also no placebo intervention in the control group. In addition, sensitization was reduced at the 8-year follow-up, suggesting that primary prevention of dust mite exposure may interfere with the development of childhood asthma.

## Conclusions

A challenge in determining the effect of environmental controls on asthma is the large number of variables involved that can influence the path from exposure to sensitization to asthma. Potential exposures must be considered at home, at day care, and at schools, while other airborne particles (eg, traffic-related pollution) also may be influential in the development of asthma. In addition, there is conflicting evidence as to whether pet and endotoxin exposure may be protective or preventive, although pet removal for pet-allergic children should be stressed. The multifaceted, randomized controlled trials highlight the beneficial outcome that can result from a primary prevention strategy, although they also highlight the difficulty in attempting to control every possible exposure in the effort to prevent sensitization. Further studies regarding remediation in schools are necessary, as is public policy change that can regulate air pollution. Simple control measures such as

mattress covers, HEPA filters, avoidance of ETS, pest control, and simple home repair may offer protection from exposure in children, but investigators should continue to explore comprehensive strategies to decrease and prevent childhood asthma.

## Acknowledgments

Dr. Phipatanakul is funded by National Institutes of Health/National Institute of Allergy and Infectious Diseases R-01 grant (AI-073964) and National Institutes of Health/National Institute of Allergy and Infectious Diseases AsthmaNet 1U10HL098102.

## References

1. Arshad SH, Tariq SM, Matthews S, et al. Sensitization to common allergens and its association with allergic disorders at age 4 years: a whole population birth cohort study. Pediatrics. 2001; 108:E33. [PubMed: 11483843]
2. Sears MR, Herbison GP, Holdaway MD, et al. The relative risks of sensitivity to grass pollen, house dust mite and cat dander in the development of childhood asthma. Clin Exp Allergy. 1989; 19:419–424. [PubMed: 2758355]
3. Wahn U, Lau S, Bergmann R, et al. Indoor allergen exposure is a risk factor for sensitization during the first three years of life. J Allergy Clin Immunol. 1997; 99:763–769. [PubMed: 9215243]
4. Sporik R, Holgate ST, Platts-Mills TA, et al. Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood. A prospective study. N Engl J Med. 1990; 323:502–507. [PubMed: 2377175]
5. Wang J, Visness CM, Calatroni A, et al. Effect of environmental allergen sensitization on asthma morbidity in inner-city asthmatic children. Clin Exp Allergy. 2009; 39:1381–1389. [PubMed: 19489919]
6. Celedon JC, Milton DK, Ramsey CD, et al. Exposure to dust mite allergen and endotoxin in early life and asthma and atopy in childhood. J Allergy Clin Immunol. 2007; 120:144–149. [PubMed: 17507083]
7. Halken S, Host A, Niklassen U, et al. Effect of mattress and pillow encasings on children with asthma and house dust mite allergy. J Allergy Clin Immunol. 2003; 111:169–176. [PubMed: 12532114]
8. de Vries MP, van den Bemt L, Aretz K, et al. House dust mite allergen avoidance and self-management in allergic patients with asthma: randomised controlled trial. Br J Gen Pract. 2007; 57:184–190. [PubMed: 17359604]
9. Woodcock A, Forster L, Matthews E, et al. Control of exposure to mite allergen and allergen-impermeable bed covers for adults with asthma. N Engl J Med. Jul 17.2003 349:225–236. [PubMed: 12867606]
10. Arshad SH, Bateman B, Sadeghnejad A, et al. Prevention of allergic disease during childhood by allergen avoidance: the Isle of Wight prevention study. J Allergy Clin Immunol. 2007; 119:307–313. [PubMed: 17291851]
11. Crane J, Kemp T, Siebers R, et al. Increased house dust mite allergen in synthetic pillows may explain increased wheezing. BMJ. 1997; 314:1763–1764. [PubMed: 9202523]
12. Hallam C, Custovic A, Simpson B, et al. Mite allergens in feather and synthetic pillows. Allergy. 1999; 54:407–408. [PubMed: 10371108]
13. Glasgow, NJ.; Ponsonby, AL.; Kemp, A., et al. Arch Dis Child. 2011. Feather bedding and childhood asthma associated with house dust mite sensitisation: a randomised controlled trial.
14. Trevillian LF, Ponsonby AL, Dwyer T, et al. Infant sleeping environment and asthma at 7 years: a prospective cohort study. Am J Public Health. 2005; 95:2238–2245. [PubMed: 16304135]
15. McDonald LG, Tovey E. The role of water temperature and laundry procedures in reducing house dust mite populations and allergen content of bedding. J Allergy Clin Immunol. 1992; 90:599–608. [PubMed: 1401643]
16. Gotzsche PC, Johansen HK. House dust mite control measures for asthma: systematic review. Allergy. 2008; 63:646–659. [PubMed: 18445182]

17. 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. [PubMed: 11590373]

18. Lau S, Illi S, Platts-Mills TA, et al. Longitudinal study on the relationship between cat allergen and endotoxin exposure, sensitization, cat-specific IgG and development of asthma in childhood—report of the German Multicentre Allergy Study (MAS 90). Allergy. 2005; 60:766–773. [PubMed: 15876306]

19. Takkouche B, Gonzalez-Barcala FJ, Etminan M, et al. Exposure to furry pets and the risk of asthma and allergic rhinitis: a meta-analysis. Allergy. 2008; 63:857–864. [PubMed: 18588551]

20. Apelberg BJ, Aoki Y, Jaakkola JJ. Systematic review: exposure to pets and risk of asthma and asthma-like symptoms. J Allergy Clin Immunol. 2001; 107:455–460. [PubMed: 11240945]

21•. Kerkhof M, Wijga AH, Brunekreef B, et al. Effects of pets on asthma development up to 8 years of age: the PIAMA study. Allergy. 2009; 64:1202–1208. [PubMed: 19245426]

22. Shirai T, Matsui T, Suzuki K, et al. Effect of pet removal on pet allergic asthma. Chest. 2005; 127:1565–1571. [PubMed: 15888829]

23. Wang C, Abou El-Nour MM, Bennett GW. Survey of pest infestation, asthma, and allergy in low-income housing. J Community Health. 2008; 33:31–39. [PubMed: 18080206]

24. Amr S, Bollinger ME, Myers M, et al. Environmental allergens and asthma in urban elementary schools. Ann Allergy Asthma Immunol. 2003; 90:34–40. [PubMed: 12546335]

25. Morgan WJ, Crain EF, Gruchalla RS, et al. Results of a home-based environmental intervention among urban children with asthma. N Engl J Med. 2004; 351:1068–1080. [PubMed: 15356304]

26. Chew GL, Perzanowski MS, Canfield SM, et al. Cockroach allergen levels and associations with cockroach-specific IgE. J Allergy Clin Immunol. 2008; 121:240–245. [PubMed: 17936887]

27. Rosenstreich DL, Eggleston P, Kattan M, et al. The role of cockroach allergy and exposure to cockroach allergen in causing morbidity among inner-city children with asthma. N Engl J Med. 1997; 336:1356–1363. [PubMed: 9134876]

28. Phipatanakul W, Eggleston PA, Wright EC, et al. Mouse allergen. II. The relationship of mouse allergen exposure to mouse sensitization and asthma morbidity in inner-city children with asthma. J Allergy Clin Immunol. 2000; 106:1075–1080. [PubMed: 11112889]

29. Phipatanakul W, Eggleston PA, Wright EC, et al. Mouse allergen. I. The prevalence of mouse allergen in inner-city homes. The National Cooperative Inner-City Asthma Study. J Allergy Clin Immunol. 2000; 106:1070–1074. [PubMed: 11112888]

30•. Sheehan WJ, Rangsithienchai PA, Muilenberg ML, et al. Mouse allergens in urban elementary schools and homes of children with asthma. Ann Allergy Asthma Immunol. 2009; 102:125–130. [PubMed: 19230463]

31. Peters JL, Levy JI, Muilenberg ML, et al. Efficacy of integrated pest management in reducing cockroach allergen concentrations in urban public housing. J Asthma. 2007; 44:455–460. [PubMed: 17654132]

32. Kass D, McKelvey W, Carlton E, et al. Effectiveness of an integrated pest management intervention in controlling cockroaches, mice, and allergens in New York City public housing. Environ Health Perspect. 2009; 117:1219–1225. [PubMed: 19672400]

33. Phipatanakul W, Cronin B, Wood RA, et al. Effect of environmental intervention on mouse allergen levels in homes of inner-city Boston children with asthma. Ann Allergy Asthma Immunol. 2004; 92:420–425. [PubMed: 15104193]

34. Seltzer JM, Fedoruk MJ. Health effects of mold in children. Pediatr Clin North Am. 2007; 54:309–333. viii–ix. [PubMed: 17448362]

35. Fisk WJ, Lei-Gomez Q, Mendell MJ. Meta-analyses of the associations of respiratory health effects with dampness and mold in homes. Indoor Air. 2007; 17:284–296. [PubMed: 17661925]

36. Mendell MJ, Mirer AG, Cheung K, et al. Respiratory and allergic health effects of dampness, mold, and dampness-related agents: a review of the epidemiologic evidence. Environ Health Perspect. 2011; 119:748–756. [PubMed: 21269928]

37. Iossifova YY, Reponen T, Ryan PH, et al. Mold exposure during infancy as a predictor of potential asthma development. Ann Allergy Asthma Immunol. 2009; 102:131–137. [PubMed: 19230464]

38. Karvonen AM, Hyvarinen A, Roponen M, et al. Confirmed moisture damage at home, respiratory symptoms and atopy in early life: a birth-cohort study. Pediatrics. 2009; 124:e329–338. [PubMed: 19651571]
39. Lignell U, Meklin T, Putus T, et al. Effects of moisture damage and renovation on microbial conditions and pupils' health in two schools—a longitudinal analysis of five years. J Environ Monit. 2007; 9:225–233. [PubMed: 17344947]
40. Kercsmar CM, Dearborn DG, Schluchter M, et al. Reduction in asthma morbidity in children as a result of home remediation aimed at moisture sources. Environ Health Perspect. 2006; 114:1574–1580. [PubMed: 17035145]
41. Parker EA, Israel BA, Robins TG, et al. Evaluation of Community Action Against Asthma: a community health worker intervention to improve children's asthma-related health by reducing household environmental triggers for asthma. Health Educ Behav. 2008; 35:376–395. [PubMed: 17761540]
42. Children and secondhand smoke exposure. Excerpts from The Health Consequences of Involuntary Exposure to Tobacco Smoke: A Report of the Surgeon General. 2007. cited; Available at http://www.surgeongeneral.gov/library/smokeexposure/report/fullreport.pdf
43. Hedman L, Bjerg A, Sundberg S, et al. Both environmental tobacco smoke and personal smoking is related to asthma and wheeze in teenagers. Thorax. 2011; 66:20–25. [PubMed: 21047869]
44. Priest N, Roseby R, Waters E, et al. Family and carer smoking control programmes for reducing children's exposure to environmental tobacco smoke. Cochrane Database Syst Rev. 2008; 4:CD001746. [PubMed: 18843622]
45. Lanphear BP, Aligne CA, Auinger P, et al. Residential exposures associated with asthma in US children. Pediatrics. 2001; 107:505–511. [PubMed: 11230590]
46. Gerald LB, Gerald JK, Gibson L, et al. Changes in environmental tobacco smoke exposure and asthma morbidity among urban school children. Chest. 2009; 135:911–916. [PubMed: 19017893]
47. Chan-Yeung M, Ferguson A, Watson W, et al. The Canadian Childhood Asthma Primary Prevention Study: outcomes at 7 years of age. J Allergy Clin Immunol. 2005; 116:49–55. [PubMed: 15990772]
48. Douwes J, van Strien R, Doekes G, et al. Does early indoor microbial exposure reduce the risk of asthma? The Prevention and Incidence of Asthma and Mite Allergy birth cohort study. J Allergy Clin Immunol. 2006; 117:1067–1073. [PubMed: 16675334]
49•. Bertelsen RJ, Carlsen KC, Carlsen KH, et al. Childhood asthma and early life exposure to indoor allergens, endotoxin and beta(1,3)-glucans. Clin Exp Allergy. 2010; 40:307–316. [PubMed: 20210808]
50. Sordillo JE, Alwis UK, Hoffman E, et al. Home characteristics as predictors of bacterial and fungal microbial biomarkers in house dust. Environ Health Perspect. 2011; 119:189–195. [PubMed: 20965804]
51. Morgenstern V, Zutavern A, Cyrys J, et al. Respiratory health and individual estimated exposure to traffic-related air pollutants in a cohort of young children. Occup Environ Med. 2007; 64:8–16. [PubMed: 16912084]
52. Braback L, Forsberg B. Does traffic exhaust contribute to the development of asthma and allergic sensitization in children: findings from recent cohort studies. Environ Health. 2009; 8:17. [PubMed: 19371435]
53. Gehring U, Wijga AH, Brauer M, et al. Traffic-related air pollution and the development of asthma and allergies during the first 8 years of life. Am J Respir Crit Care Med. 2010; 181:596–603. [PubMed: 19965811]
54. Gupta RS, Ballesteros J, Springston EE, et al. The state of pediatric asthma in Chicago's Humboldt Park: a community-based study in two local elementary schools. BMC Pediatr. 2010; 10:45. [PubMed: 20576150]
55. Miller RL, Chew GL, Bell CA, et al. Prenatal exposure, maternal sensitization, and sensitization in utero to indoor allergens in an inner-city cohort. Am J Respir Crit Care Med. 2001; 164:995–1001. [PubMed: 11587985]
56. Chang C, Gauvey-Kern K, Johnson A, et al. Cord blood versus age 5 mononuclear cell proliferation on IgE and asthma. Clin Mol Allergy. 2010; 8:11. [PubMed: 20684781]

57. Chan-Yeung M, Dimich-Ward H, Becker A. Atopy in early life and effect of a primary prevention program for asthma in a high-risk cohort. J Allergy Clin Immunol. 2007; 120:1221–1223. [PubMed: 17919706]