



From the Pages of allergywatch®

Recent advances in our understanding of the environment's role in allergy



Chitra Dinakar, MD ^{*,†,‡}; Stanley M. Fineman, MD ^{*,§}; Bradley E. Chipps, MD ^{*,§,**}; David A. Khan, MD ^{*,††}; Stephen A. Tilles, MD ^{*,‡‡}

^{*} AllergyWatch, Sacramento, California

[†] Medicine, Pulmonary & Critical Care Medicine, Stanford University, Stanford, California

[‡] Asthma and Immunodeficiency, Stanford Health Care, Stanford, California

[§] Atlanta Allergy & Asthma, Marietta, Georgia

[§] American College of Allergy, Asthma & Immunology, Arlington Heights, Illinois

^{**} Capital Allergy & Respiratory Disease Center, Sacramento, California

^{††} Division of Allergy & Immunology, University of Texas Southwestern Medical School, Dallas, Texas

^{‡‡} Northwest Asthma & Allergy Center, Redmond, Washington

A new *Annals* feature in 2018, “From the pages of AllergyWatch” is devoted to publishing synopses of Allergy and Asthma literature relevant to a topic of emphasis. These unbiased synopses and comments by our Editors have been previously printed in the

AllergyWatch bimonthly newsletter, and it is our hope that presenting carefully selected article summaries and comments in the *Annals* will serve as a valuable educational resource for practicing allergists.

Fixing Indoor Air Quality Can Improve Asthma

The indoor environment can have a major impact on asthma morbidity in children. Indoor exposures include not only allergens such as dust mite but also pollutants such as secondhand smoke. This report highlights the role of indoor environmental control practices in the management of childhood asthma. Environmental control measures should be tailored to the individual child, based on knowledge of allergic sensitivities and relevant indoor exposures. An environmental history can be performed, addressing key exposures known to trigger the child's asthma symptoms and exacerbations. The presence of furred pets and indoor pests should be evaluated; dust mite exposure is a factor in all but arid environments. In addition to the presence of smokers in the household, evaluation of indoor pollutants should address the use of gas stoves and other appliances. Specific IgE testing, or referral to an allergist for skin testing, can guide efforts to identify the clinically relevant indoor allergens. The report provides information on specific allergens, including dust mite, pets, rodents, cockroach, and dampness and mold; as well as indoor pollutants, including particulate matter, secondhand smoke, and nitrogen dioxide. Environmental control measures include removal or control of the exposure source, as well as mitigation measures such as

high-efficiency particulate air purifiers and allergen-proof mattress and pillow covers. Education may be provided by primary care clinicians or specialists or by trained community health workers. The report outlines the importance of indoor exposures in childhood asthma, including evaluation and control measures for indoor allergens and pollutants. The authors point out that public and private insurance generally do not cover the cost of environmental assessment and control measures, despite evidence of their cost-effectiveness.

Comments from Chitra Dinakar, MD: This excellent clinical report emphasizes that indoor allergens and pollutants are major contributors to asthma morbidity. Some tailored environmental control practices can reduce asthma symptoms and exacerbations, with comparable efficacy and cost to controller medications. Strategies that can be delivered by primary care physicians, specialists, and other health care workers are discussed.

Matsui EC, Abrahamson SL, Sandel MT
Indoor environmental control practices and
asthma management.
Pediatrics. 2016;138(5):e20162589.

Reprints: Stephen A. Tilles, MD, Northwest Asthma & Allergy Center, 8301 161st Ave. NE, Suite 308, Redmond, WA 98052; E-mail: stilles@nwasthma.com.

Disclosures: Dr. Dinakar reports consultant/advisory to Aerocrine, Aimmune, Boehringer Ingelheim, Food Allergy Research & Education (FARE), GlaxoSmithKline, Merck, Teva. Dr. Fineman reports research grants from: Aimmune, Genentech, Meda, Stallergenes, Teva; and consultant/advisory to Greer, Mylan, Teva. Dr. Chipps reports consultant/advisory to AstraZeneca, Boehringer Ingelheim, Genentech, Novartis, Meda, Merck. Dr. Khan reports Speaker/Teacher fees from Genentech and Consultant/Advisor fees from Aimmune. Dr. Tilles reports research grants from: Amgen, Astellas, AstraZeneca, Boehringer Ingelheim, Circassia, DBV Technologies, Genentech, Immune Tolerance Network (NIH), Merck, Mylan, Novartis, Pulmagen, Stanford Univ., Gilead, Teva, Aimmune, Biota; and consultant/advisory to Food Allergy Research & Education (FARE) and Immune Tolerance Network (NIH).

<https://doi.org/10.1016/j.anaai.2018.03.025>

1081-1206/© 2018 American College of Allergy, Asthma & Immunology. Published by Elsevier Inc. All rights reserved.

Traffic-Related Air Pollution – Bad for Allergic Adults Too!

Previous studies have shown reduced lung function and an increased risk of allergic respiratory diseases in children with higher exposure to traffic-related air pollution (TRAP). Less is known about the effects of TRAP in adults. This study examined the association between TRAP exposure, asthma, and other respiratory outcomes in middle-aged adults in a low-pollution area. The analysis included subjects from the Tasmanian Longitudinal Health Study, enrolled as children in 1968. In their forties, 1,405 adults participated in a laboratory study including skin prick and lung function testing. Each subject's mean annual residential nitrogen oxide exposure was calculated based on their current residential address. Exposure to TRAP was evaluated for associated with allergic sensitization, lung function, current wheezing, and asthma. Higher NO₂ exposure was associated with an increased risk of atopy, adjusted odds ratio (OR) 1.14 per 1 interquartile range increase; and current wheezing, OR 1.14. Subjects who lived within 200 m of a major road had higher rates of atopy and current wheezing: OR 1.26 and 1.38, respectively. Living near a major road was also associated with decreased lung function, including pre- and postbronchodilator FEV₁ and prebronchodilator FEF 25–75% of forced vital capacity. Living near a major road also interacted with the glutathione S-transferase gene to affect the risk of asthma and allergic disease outcomes. Carriers of the GSTT1 null genotype were at higher risk of atopy, asthma,

and atopic asthma with higher TRAP exposure. Even at relatively low levels, TRAP exposure is associated with atopy, asthma, and reduced lung function in middle-aged adults. These risks appear particularly high in individuals with the GSTT1 null genotype. This finding may have important public health implications for a genetically susceptible population.

Comments from Stanley Fineman, MD: Air pollution, particularly TRAP, causes oxidative damage to airways and inflammation and enhances allergic reactions. Although this association is well-documented in children, this unique study shows that it is also present in adults. The researchers not only measured allergy skin tests, lung function, and symptoms but also analyzed GST genes, which play an important role in modulating inflammation. Even though nitrogen dioxide exposures in Australia were lower than in North America and Europe, there was still a significant increase in allergy among adults living less than 200 m from a major road—especially for carriers of the GSTT1 null genotype.

Bowatte G, Lodge CJ, Knibbs LD, et al.
Traffic-related air pollution exposure is associated with allergic sensitization, asthma, and poor lung function in middle age.

J Allergy Clin Immunol. 2017;139:122–129.

Polluted Air Kills

Long-term exposure to air pollution is associated with increased mortality. There are limited data on the effects of air pollution levels below current air quality standards or outside of urban areas. This study used Medicare data to assess the relationship between long-term air pollution exposure and mortality in older adults. The cohort study included 61 million Medicare beneficiaries in the continental United States from 2000 through 2012, with more than 460 million person-years of follow-up. Annual average exposures to PM_{2.5} and ozone were calculated using validated prediction models. Associations between pollutant exposure and death were assessed with adjustment for demographic factors, Medicaid eligibility, and area-level covariates. The results showed pollutant-related increases in mortality at levels below national standards. All-cause mortality increased by 7.3% per 10 mg increase in PM_{2.5} exposure and by 1.1% per 10 ppb in ozone exposure. On analysis limited to years of exposure to low pollutant levels—12 m/m³ for PM_{2.5} and 50 ppb for ozone—risk of death increased by 13.6% and 1.0%, respectively. The mortality impact of PM_{2.5} exposure was greater for men, black subjects, and those eligible for Medicaid. Long-term exposure to particulate air pollution and ozone is associated with increased mortality in the Medicare population. These health effects are observed at

exposure levels below current national air quality standards and are greater in racial minorities and disadvantaged groups. The authors discuss the implications for determining the health effects of low levels of air pollution and for setting air-quality standards.

Comments from Chitra Dinakar, MD: This eye-opening, decade-long cohort study involved 61 million Medicare beneficiaries. It showed that long-term exposures to PM_{2.5} and ozone were associated with an increased risk of death. Even more starkly, the increased risk was seen at levels below the current established safe standards! These findings have profound implications for regulatory health policy that can have important public health benefits. Allergists should rally together to work towards the goal of reducing air pollution. That's despite the sobering insight expressed in the provocative editorial by Berger et al (*N Engl J Med* 2017; 376:2591–2592), that "Ironically, Pittsburgh is less than 30 miles from the Donora Smog Museum, where a sign reads 'Clean Air Started Here.'"

Di Q, Wang Y, Zanobetti A, et al.
Air Pollution and mortality in the Medicare population.
N Engl J Med. 2017;376:2513–2522.

Dust Mite Avoidance Works After All

Many children with asthma are sensitized to house dust mite (HDM). Allergen exposure, in synergy with viral infection, is an important risk factor for exacerbation and hospital admission. This randomized trial evaluated the benefits of mite-impermeable bedcovers for HDM-sensitized children with asthma. The UK study included 284 mite-sensitized children with asthma exacerbations who were seen in the emergency department (ED). More than two-thirds of the children were boys; mean age was 7.7 years. Patients were randomized to receive a mite-impermeable bedcover or a control/placebo bedcover. At 12 months, the occurrence of severe asthma exacerbations was compared between groups. Children who received mite-impermeable bedcovers had a lower rate of emer-

gency department visits for asthma exacerbation: 29.3%, compared to 41.5% for those receiving placebo bedcovers. On multivariable analysis, the hazard ratio for hospital visits for exacerbations was 0.55 in the active treatment group. There was also a 27% reduction in ED visits, but the difference was not significant. There was also no difference in exacerbations requiring prednisolone. Levels of Der p 1 in mattress dust were 84% lower for children receiving mite-impermeable bedcovers. Allergen-impermeable bedcovers can reduce ED visits for exacerbations in asthmatic children with HDM allergy. The bedcovers cost about \$200; the authors estimate that providing 8 children with mite-impermeable bedcovers would prevent one patient from a hospital visit in the subsequent year.

Comments from Bradley Chipps, MD: Childhood asthma is associated with a high rate of HDM allergy. When mites are controlled, bronchial hyperreactivity decreases. In the present study, this strategy resulted in a highly significant decrease in levels of major HDM allergen (Der p 1). There was a 45% decrease in exacerbations requiring acute treatment compared to placebo. However, there was no statistically significant difference regarding the use of prednisone.

lone. This “one-time,” low-cost intervention does not require prior authorization or co-pays and should be discussed with patients.

Murray CS, Foden P, Summer H, et al.
Preventing severe asthma exacerbations in children:
a randomized trial of mite-impermeable bedcovers.
Am J Respir Crit Care Med. 2017;196:150–158.

Probiotics in Your Mattress Cover...Really?

Allergen avoidance is commonly recommended for patients with allergic rhinitis (AR) and house dust mite allergy. Previous trials of impermeable bedding covers, alone or with other avoidance measures, have shown little benefit in reducing AR symptoms. This pilot study evaluates a new type of bedding cover impregnated with probiotics. The trial included 20 adults with AR, with confirmed house dust mite allergy and presence of Der p 1 in bedding dust samples. In crossover fashion, patients used Purotex bedding covers and untreated placebo bedding covers for 8 weeks. The two bedding covers led to similar reductions in Der p 1 in mattress and pillow dust samples, the primary study outcome. The probiotic-impregnated bedding covers also led to improvement in some AR symptom and quality of life (QOL) scores compared to baseline, which were not observed with the untreated covers. However, the differences in these outcomes were not significantly different between the intervention and control periods. The results show significant improvement in some AR symptoms and QOL scores with probiotic-impregnated bedding covers for patients

with house dust mite allergy. This is despite the lack of difference in Der p 1 levels. A larger trial might show a significant difference in clinical outcomes.

Comments by David Khan, MD: Studies of bedding covers have been somewhat disappointing in reducing AR symptoms. In laboratory studies, probiotics have reduced Der p 1 levels in fabrics. This small study evaluated clinical effects of probiotic-impregnated bedding covers. Mite allergen levels were reduced in both encasement groups. Although symptoms and QOL were better with probiotics compared to baseline, there was no difference between probiotic and standard encasements. While the study is small, the results are not very impressive and suggest that enhancing encasements with probiotics is of little benefit.

Berings M, Jult A, Vermeulen H, et al.
Probiotics-impregnated bedding covers for house dust mite
allergic rhinitis: a pilot randomized clinical trial.
Clin Exp Allergy. 2017;47:1092–1096.

Farm Exposure Linked to Lower Adult Atopy Risk

Previous studies have linked growing up on a farm to a reduced risk of childhood allergy and asthma. Most of these studies have been performed in Europe, while few have examined the allergic disease outcomes in adults. The effects of early-life farm exposure on adult asthma and atopy were assessed in US cohort study. The Agricultural Lung Health Study included 1,746 farmers and 1,555 spouses, mean age 63 years, from a larger US agricultural cohort. Participants provided information on early-life farming exposure and current asthma in questionnaires; atopy was assessed by measurement of specific IgE levels. Associations between early-life farm exposure and asthma (1,198 cases versus 2,031 controls) and atopy (578 cases and 2,526 controls) were examined by logistic regression, adjusted for age, sex, race, state, and smoking. Farm exposure in utero and during early childhood was unrelated to asthma in adulthood. However, there were significant protective effects against atopy. The strongest association, odds ratio 0.60, was noted for participants whose mothers performed farm tasks during pregnancy. Reductions in adult atopy with early-life farm exposure remained significant after considering contact with farm animals, raw milk consumption, and other early exposures. This US study finds a lower

risk of atopy among older adults exposed to a farm environment during early-life. The findings support the role of in utero and early childhood exposures in the development of allergic disease. Early-life farm exposure appears to have a lifelong protective effect against atopy, but not asthma.

Comments by Stanley Fineman, MD: Previous studies of early-life farm exposures have generally shown a protective effect against allergies and asthma in children. This is the first report to study atopy and asthma in adults in relation to early-life farming exposures. Although farm exposure had little impact on adult asthma, there was some protective effect against adult atopy. Interestingly, having a mother performing farm activities while pregnant reduced the odds of adult atopy. It seems the protective effect of early-life farming exposures may begin in utero and endure into adulthood.

House JS, Wyss AB, Hoppin JA, et al.
Early-life farm exposures and adult asthma and atopy in the
Agricultural Lung Health Study.
J Allergy Clin Immunol. 2017;140:249–256.