

Free Executive Summary



Clearing the Air: Asthma and Indoor Air Exposures

Committee on the Assessment of Asthma and Indoor Air, Division of Health Promotion and Disease Prevention, Institute of Medicine

ISBN: 978-0-309-06496-5, 456 pages, 6 x 9, hardback (2000)

This free executive summary is provided by the National Academies as part of our mission to educate the world on issues of science, engineering, and health. If you are interested in reading the full book, please visit us online at <http://www.nap.edu/catalog/9610.html>. You may browse and search the full, authoritative version for free; you may also purchase a print or electronic version of the book. If you have questions or just want more information about the books published by the National Academies Press, please contact our customer service department toll-free at 888-624-8373.

Since about 1980, asthma prevalence and asthma-related hospitalizations and deaths have increased substantially, especially among children. Of particular concern is the high mortality rate among African Americans with asthma. Recent studies have suggested that indoor exposures--to dust mites, cockroaches, mold, pet dander, tobacco smoke, and other biological and chemical pollutants--may influence the disease course of asthma. To ensure an appropriate response, public health and education officials have sought a science-based assessment of asthma and its relationship to indoor air exposures. Clearing the Air meets this need. This book examines how indoor pollutants contribute to asthma-- its causation, prevalence, triggering, and severity. The committee discusses asthma among the general population and in sensitive subpopulations including children, low-income individuals, and urban residents. Based on the most current findings, the book also evaluates the scientific basis for mitigating the effects of indoor air pollutants implicated in asthma. The committee identifies priorities for public health policy, public education outreach, preventive intervention, and further research.

This executive summary plus thousands more available at www.nap.edu.

Copyright 2007 © National Academy of Sciences. All rights reserved. Unless otherwise indicated, all materials in this PDF file are copyrighted by the National Academy of Sciences. Distribution or copying is strictly prohibited without permission of the National Academies Press <http://www.nap.edu/permissions/> Permission is granted for this material to be posted on a secure password-protected Web site. The content may not be posted on a public Web site.



EXECUTIVE SUMMARY

The statistics are disturbing.

The Centers for Disease Control and Prevention (CDC) estimates that asthma affected about 17.3 million individuals in the United States in 1998. It is the most common chronic illness among children in the United States and one of the most common chronic illnesses overall in the country. Although by many measures the health of Americans is improving, CDC notes the self-reported prevalence rate for asthma increased 75% from 1980 to 1994. Studies show that asthma mortality is disproportionately high among African Americans and in urban areas that are characterized by high levels of poverty and minority populations. Nor is the phenomenon limited to the United States. The prevalence of asthma in some other parts of the world—including Australia, New Zealand, Ireland, and the United Kingdom—exceeds that of the United States.

Researchers have wondered whether the indoor environment may play a role in the increasing asthma problem. There is ample justification for this speculation. We know, for example, that individuals spend nearly all of their time indoors—most of it in their own homes—and that many of the exposures thought to be associated with asthma occur predominately indoors. If the indoor

environment plays a role, then interventions to limit or eliminate exposures there have the potential to help asthmatics and perhaps result in primary prevention of the illness.

Against this backdrop, the U.S. Environmental Protection Agency (EPA) is developing an outreach strategy focused on reducing asthma-related morbidity and mortality potentially associated with exposure to indoor environments. To help ensure that such efforts are based on sound science, EPA requested that the National Academies undertake an assessment of asthma and its relationship to indoor air quality. The EPA charged the committee with two primary objectives:

1. To provide the scientific and technical basis for communications to the public on the health impacts of indoor pollutants related to asthma, and mitigation and prevention strategies to reduce these pollutants.
2. To help determine what research is needed in these areas.

This report presents the results of that assessment.

ORGANIZATION AND FRAMEWORK

The content of this report reflects the committee's goal to speak to a wide-ranging audience of science, health, and engineering professionals; government officials; and interested members of the public. The material presented thus covers a broad range of topics in order to establish a common base of knowledge for the reader. The scope of this material is far too vast for any one book to deal with comprehensively. Other publications, cited throughout the report, go into greater detail on specific issues.

The major topics addressed in the report are the following:

- the definition of asthma and the characteristics of its clinical presentation (Chapter 1);
- methodologic issues in evaluating the evidence regarding indoor air exposures and asthma, including the categorizations used to summarize the evidence and the framework for considering exposure to indoor sources (Chapter 2);

TABLE 1 Indoor Exposures Addressed in This Report

Biological	
Animals	Fungi or molds
Cats	Houseplants
Dogs	Pollen
Rodents	Infectious agents
Cows and horses	Rhinovirus
Domestic birds	Respiratory syncytial virus
Cockroaches	<i>Chlamydia trachomatis</i>
House dust mites	<i>Chlamydia pneumoniae</i>
Endotoxins	<i>Mycoplasma pneumoniae</i>

Chemical	
NO ₂ , NO _x (nitrogen oxides)	Plasticizers
Pesticides	Volatile organic compounds
Ozone*	Formaldehyde
Particulate matter with sources other than ETS*	Fragrances
SO ₂ , SO _x (sulfur oxides)*	Environmental Tobacco Smoke (ETS)

*An outdoor air pollutant potentially associated with asthma that can penetrate the indoor environment and that may in some cases have indoor sources. Since the committee's mandate was to address indoor air pollutants, the discussion of this agent is less detailed than others in the report and no conclusions are drawn concerning outdoor exposures and asthma outcomes.

- patterns of asthma morbidity and mortality (Chapter 3);
- the pathophysiology of asthma—that is, the molecular mechanisms that underlie the structural and functional changes in the lungs and airways of asthmatics (Chapter 4);
- the committee's review of the state of the scientific literature regarding indoor air exposures and the exacerbation and development of asthma—Table 1 lists the biologic and chemical exposures addressed in this report. (Chapters 5–7);
- the scientific literature on general exposures in indoor environments (Chapters 8–9); and
- how indoor exposures to pollutants associated with the incidence or symptoms of asthma are affected by building ventilation and particle air cleaning (Chapter 10).

The committee faced a significant challenge in conducting its review—research on asthma is burgeoning and significant new papers are constantly being published. Although the committee did its best to paint an accurate picture of the state of the science at the time the report was completed, it is inevitable that research advances will overtake its conclusions.

CONCLUSIONS ABOUT THE RELATIONSHIP BETWEEN INDOOR EXPOSURES AND ASTHMA

The committee used a uniform set of categories to summarize its conclusions regarding the association between exposure to an indoor agent and asthma development and exacerbation, and the effectiveness of exposure mitigation and prevention measures. Box 1 lists the definitions of these categories. The distinctions among categories reflect the committee's judgment of the overall strength, quality, and persuasiveness of the scientific literature evaluated. Chapter 2 details the methodologic considerations underlying the categorizations and their definitions.

The sections below are a synopsis of the committee's findings. Chapters 5 through 10 address the reasoning underlying the conclusions and present the findings in greater detail.

Exposure Settings

The indoor exposures considered in this report are highly dependent on the characteristics of the outdoor and indoor environment and its occupants. For example, house dust mites are a very common exposure in temperate and humid regions. They are found primarily within residences, concentrated in the bedroom. Cockroaches, which also thrive in temperate and humid regions, are an important exposure in some urban environments. They are found primarily near food sources. Fungi are ubiquitous and have been the primary source of allergen for several studied populations. Endotoxins may be found in humidifiers and in bacteria from other indoor, as well as outdoor sources. In some environments, exposure to animal allergens; molds; environmental tobacco smoke (ETS); indoor combustion products; and chemicals used in cleaning, building materials, and furnishings may be im-

BOX 1

Categories of Evidence Used in This Report

Sufficient Evidence of a Causal Relationship

Evidence is sufficient to conclude that a causal relationship exists between the action or agent and the outcome. That is, the evidence fulfills the criteria for “Sufficient Evidence of an Association” below and in addition satisfies criteria regarding the strength of association, biologic gradient (dose–response effect), consistency of association, biologic plausibility and coherence, and temporality used to assess causality.

Sufficient Evidence of an Association

Evidence is sufficient to conclude that there is an association. That is, an association between the action or agent and the outcome has been observed in studies in which chance, bias, and confounding can be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence of an association.

Limited or Suggestive Evidence of an Association

Evidence is suggestive of an association between the action or agent and the outcome but is limited because chance, bias, and confounding cannot be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent.

Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists

The available studies are of insufficient quality, consistency, or statistical power to permit a conclusion regarding the presence or absence of an association; or no studies exist that examine the relationship. For example, available studies have failed to adequately control for confounding or have inadequate exposure assessment.

Limited or Suggestive Evidence of No Association

Several adequate studies are mutually consistent in not showing an association between the action or agent and the outcome. A conclusion of “no association” is inevitably limited to the conditions, level of exposure, and length of observation covered by the available studies. *In addition, the possibility of a very small elevation in risk at the levels of exposure studied can never be excluded.*

portant. Many of these pollutants are also present in outdoor air, and indoor exposures can result from the infiltration of outdoor air into buildings.

Indoor Air Exposures and Asthma Exacerbation

Studies of asthma can be divided into those dealing with factors leading to the development of asthma and those dealing with factors that exacerbate the illness in known asthmatics. Most of the research on this topic addresses “asthma exacerbation,” the onset or worsening of symptoms—some combination of shortness of breath, cough, wheezing, and chest tightness—in someone who already has developed asthma.

Epidemiologic investigations, challenge studies, and clinical experience have yielded solid information on the potential for many indoor exposures to exacerbate asthma. The committee found **sufficient evidence to conclude that there is a causal relationship** between

- exposure to the allergens produced by cats, cockroaches, and house dust mites, and exacerbations of asthma in sensitized individuals; and
- ETS exposure and exacerbations of asthma in preschool-aged children.

There is **sufficient evidence of an association** between several exposures and exacerbations of asthma. Dog allergen exposure is associated with exacerbation of asthma in individuals specifically sensitized to these allergens. Fungal exposure is associated with exacerbation in sensitized asthmatics and may be associated with nonspecific chest symptoms. Research indicates that rhinovirus infection is associated with wheezing and exacerbations in asthmatics. There is also sufficient evidence to conclude that brief high-level¹ exposures to NO₂ and increased airway responses among asthmatic subjects to both nonspecific chemical irritants and inhaled allergens.

¹At concentrations that may occur only when gas appliances are used in poorly ventilated kitchens.

Damp conditions are associated with the presence of symptoms considered to reflect asthma; symptom prevalence among asthmatics is also related to dampness indicators. The factors related to dampness that may actually lead to asthma exacerbation are not yet confirmed, but probably relate to dust mite and fungal allergens. There is sufficient evidence that some nonresidential buildings provide exposures that exacerbate asthma. However, the specific agents responsible for such exacerbations are as yet unstudied.

Limited or suggestive evidence was found for an association between exposures to domestic birds and exacerbation of asthma, although it is unclear what portion of this association is attributable to an allergic asthmatic response to the mites harbored by these birds. There is also limited or suggestive evidence of a relationship between

- exposure to the infectious agents respiratory syncytial virus (RSV), *Chlamydia pneumoniae*, and *Mycoplasma pneumoniae*, and exacerbation of asthma;
- chronic ETS exposure and exacerbation of asthma in older children and adults;
- acute ETS exposure and exacerbation of asthma in individuals responsive to this exposure;
- nonacute, nonoccupational formaldehyde exposure and wheezing and other respiratory symptoms; and
- exposure to certain fragrances and the manifestation of respiratory symptoms in asthmatics sensitive to such exposures.

Inadequate or insufficient information was identified to determine whether or not exacerbations of asthma result from nonacute, nonoccupational exposures to cow, horse, and rodent allergens; endotoxins; houseplants² or cut flowers; the bacterial agent *Chlamydia trachomatis*; pesticides; plasticizers; and volatile organic compounds (VOCs) other than formaldehyde. Some of these same agents do or may play a role in asthma resulting from

²Mites and fungi associated with houseplants could be involved in asthma outcomes but no studies document this connection.

exposures in occupational settings, a topic outside the purview of this study.

Although there is sufficient evidence to conclude that pollen exposure is associated with exacerbation of existing asthma in sensitized individuals, and pollen allergens have been documented in both dust and indoor air, there is inadequate or insufficient information to determine whether *indoor* exposure to pollen is associated with exacerbations of asthma.

These findings are summarized in Table 2.

Indoor Air Exposures and Asthma Development

The second outcome reviewed by the committee was the development of asthma—the initial onset of the illness. Asthma is defined by the manifestation of a set of symptoms rather than by any one objective test. With asthma symptoms ranging from clearly episodic to nearly continuous, from mild to severe, and from coughing without other respiratory symptoms to a loud wheeze, the initial diagnosis of the illness can be complicated and subject to controversy. It is thus difficult to study the determinants of and influences on asthma development. An additional complication stems from the fact that some of the most provocative evidence regarding development comes from studies of infants. Prior to the age of approximately 3, children may exhibit symptoms that are characteristic of asthma, but they may not exhibit persistent asthmatic symptoms or other related conditions such as bronchial reactivity or allergy later in life. Chapter 1 discusses the definitions of asthma and the characteristics of its clinical presentation.

Saying that a particular agent may be associated with the development of asthma does not mean it is the sole factor determining whether an individual will manifest the illness. Most scientists believe that some individuals have a prior, underlying predisposition that permits the evolution of clinical asthma. The development of this predisposition to asthma is dependent on a complex—and at present poorly understood—combination of factors, which are partially inherited and partially acquired later in life.

After careful consideration of the scientific literature, the com-

TABLE 2 Summary of Findings Regarding the Association Between Indoor Biologic and Chemical Exposures and the *Exacerbation* of Asthma in Sensitive Individuals

Biological Agents	Chemical Agents
Sufficient Evidence of a Causal Relationship	
Cat	ETS (in preschool-aged children)
Cockroach	
House Dust Mite	
Sufficient Evidence of an Association	
Dog	NO ₂ , NO _x (high-level exposures*)
Fungi or molds	
Rhinovirus	
Limited or Suggestive Evidence of an Association	
Domestic birds	ETS (in school-aged and older children, and in adults)
<i>Chlamydia pneumoniae</i>	
<i>Mycoplasma pneumoniae</i>	Formaldehyde
Respiratory Syncytial Virus (RSV)	Fragrances
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists	
Cow and horse	Pesticides
Rodents (as pets or feral animals)	Plasticizers
<i>Chlamydia trachomatis</i>	VOCs
Endotoxins	
Houseplants	
Pollen exposure in indoor environments	
Insects other than cockroaches	
Limited or Suggestive Evidence of No Association (no agents met this definition)	

*At concentrations that may occur only when gas appliances are used in poorly ventilated kitchens

mittee concluded there is **sufficient evidence of a causal relationship** between exposure to house dust mite allergen and the development of asthma in susceptible children. This conclusion was based on the preponderance of several lines of evidence, including the results of clinical studies and population-based, case-control, and prospective epidemiologic investigations; the consis-

tency of the association in different racial and ethnic groups; and the presence of a dose–response relationship between exposure to dust mite allergen and sensitization. Chapter 5 delineates the reasoning underlying this conclusion in greater detail.

There is **sufficient evidence to conclude that there is an association** between ETS exposure and the development of asthma in younger children. In the limited number of studies that have been able to separate the effects of maternal active smoking during pregnancy from the effects of ETS exposure after birth, evidence suggests that—although both exposures are detrimental—maternal smoking during pregnancy has the stronger adverse effect.

Limited or suggestive evidence exists for associations between

- cockroach allergen exposure and development of asthma in preschool-aged children; and
- infection with RSV and development of asthma in preschool-aged children.

The impact of exposure to these agents has been the subject of great research interest in the past few years, and efforts presently under way may clarify their role in asthma development.

Published case reports, public health surveillance of physician reporting, and cross-sectional studies of building occupants with indoor air quality complaints also provide limited or suggestive evidence of an association between aspects of the nonindustrial indoor environment and the development of asthma, with a building occupancy-related pattern of symptoms and in some instances objective abnormalities. What is lacking for the most part, however, is knowledge of specific etiologic agents in these nonindustrial indoor environments that might be responsible for new work-related asthma cases.

Inadequate or insufficient evidence exists to determine whether or not the other indoor exposures listed in Table 1 are associated with the development of asthma. This lack of information points to a gap in present-day knowledge concerning asthma—one that will be challenging to resolve.

There is **limited or suggestive evidence of no association** be-

tween infection with rhinovirus—the medical term for the large and ubiquitous group of viruses responsible for a variety of respiratory infections including those referred to as “the common cold”—and asthma development.

Table 3 summarizes these findings.

TABLE 3 Summary of Findings Regarding the Association Between Indoor Biologic and Chemical Exposures and the *Development* of Asthma

Biologic Agents	Chemical Agents
Sufficient Evidence of a Causal Relationship	
House dust mite	(no agents met this definition)
Sufficient Evidence of an Association	
(no agents met this definition)	ETS (in preschool-aged children)
Limited or Suggestive Evidence of an Association	
Cockroach (in preschool-aged children)	(no agents met this definition)
Respiratory Syncytial Virus (RSV)	
Inadequate or Insufficient Evidence to Determine Whether or Not an Association Exists	
Cat	NO ₂ , NO _x
Cow and horse	Pesticides
Dog	Plasticizers
Domestic birds	VOCs
Rodents	Formaldehyde
Cockroaches (except for preschool-aged children)	Fragrances
Endotoxins	ETS (in school-aged and older children, and in adults)
Fungi or molds	
<i>Chlamydia pneumoniae</i>	
<i>Chlamydia trachomatis</i>	
<i>Mycoplasma pneumoniae</i>	
Houseplants	
Pollen	
Limited or Suggestive Evidence of No Association	
Rhinovirus (adults)	(no agents met this definition)

Effectiveness of Indoor Environmental Interventions in Limiting Exposures and Affecting Asthma Outcomes

Patients with asthma and the parents of children with asthma need reliable information on which measures are likely to be most effective for improving indoor air quality. Specific recommendations are found in each chapter but there are general principles that should be kept in mind. Agents that can exacerbate asthma may generally be thought of in two categories: specific allergens and nonspecific respiratory tract irritants. Exposure to nonspecific irritants, such as cigarette smoke, may lead to asthma symptoms in any person with asthma; while allergens are only problems for individuals who are allergic to them. For example, if a person with asthma is allergic to cats, exposure to cats may cause wheezing; but if that person is not allergic to cats, exposure to them will not cause any problems. Therefore, reducing indoor airborne exposure to irritants is likely to help all asthmatic individuals to some degree while reductions in allergen exposure would only be expected to help individuals who are allergic to the allergens being reduced.

While the report identifies a number a mitigation strategies that are or may be effective in reducing exposure to potentially problematic agents, the committee found only a small number for which there is presently evidence that proper implementation of the strategy results in an improvement of symptoms or lung function in asthmatics. It is important to remember, though, that the absence of evidence does not mean an absence of effect. The science regarding indoor environmental interventions, exposure limitation, and effects on asthma outcomes is not nearly as well developed as that regarding the health effects of exposures. Exposure assessment³ is often the weakest link in environmental health studies because it is difficult to do and is given inadequate attention by many researchers.

³Classically, "exposure assessment" involves specifying the population that might be exposed to the agent of concern; identifying the routes through which exposure can occur, and estimating the magnitude, duration, and timing of the dose that individuals might receive as a result of their exposure (NAS, 1994).

Nonetheless, the committee was able to identify well-conducted, rigorous studies on which to base conclusions.

Sufficient evidence of an association was found between the use of a combination of physical measures and a reduction in indoor **dust mite** allergen levels in dust samples. As detailed in Chapter 5, strategies for the effective control of mite growth vary by climate. Such measures have been shown to be effective at reducing symptoms in controlled trials and should be part of normal management of asthma in mite-allergic individuals. Several studies now under way are evaluating whether aggressive allergen avoidance regimes have an effect on the subsequent development of asthma. The results of these and other studies will inform the question of whether primary prevention of dust mite-induced asthma is possible. Two related issues that will have to be addressed are (1) the feasibility of implementing such comprehensive interventions and (2) whether these interventions result in lower rates of sensitization to a particular exposure or all exposures.

The committee found limited or suggestive evidence that the combined use of **cockroach** extermination and control of potential reservoirs of allergen in beds, carpets, furnishings, and clothing through cleaning can achieve a short-term decrease in cockroach allergen levels in indoor environments. Extermination alone appears ineffective because significant allergen levels remain in settled dust; cleaning alone in the absence of complete extermination does not eliminate the sources of the allergen. There was inadequate or insufficient evidence to determine whether or not an association exists between any cockroach mitigation or prevention strategy and transient or long-term improvement of symptoms or lung function in cockroach-allergic asthmatics. However, since evidence does suggest that dust mite mitigation strategies result in improvement of symptoms or lung function, mitigation of cockroach exposures would appear to be a sensible course of action in the absence of more definitive information.

Although the strategy may be unpopular, there is limited or suggestive evidence of an association between removal of a **cat** from the home and improvement of symptoms or lung function in cat-allergic asthmatics. Concomitant removal or isolation of known reservoirs of cat allergen (carpets, upholstery, mattresses,

pillows) may be required to diminish allergen levels to those commonly measured in homes without cats. Limited or suggestive evidence indicates that some measures short of removal (e.g., washing the animal) may result in transient reduction in allergen levels. However, there is inadequate or insufficient evidence to determine whether or not an association exists between measures short of removal of a cat from the home and improvement in symptoms in cat-allergic asthmatics. Data on the effectiveness of interventions for **other animals** are too sparse to draw informed conclusions.

It is possible to physically remove accessible growing **fungi** from indoor environments. The entry of fungal spores from outdoors can be substantially reduced in mechanically ventilated buildings by pressurizing them and filtering incoming air; closing windows should also reduce indoor concentrations from outdoor sources. Although there is limited or suggestive evidence that such steps may result in a reduction in the levels of fungi in the indoor environment, the health impact of such reduction has not been studied. Fungi are difficult to kill, and dead fungal material probably contains allergens that can become airborne, although this has not been thoroughly tested.

There is relatively little information on the impact of ventilation and air-cleaning measures on indoor **pollen** levels, although it is clear that shutting windows and other measures that generally limit the entry rate of unfiltered outdoor air can be effective.

No general conclusions about means of altering exposure to low levels of **endotoxin** can be made at the present time. However, avoiding the use of cool mist humidifiers would appear to be a simple and effective means of eliminating risk of high-level exposure to endotoxin at home as well as exposure to organisms associated with hypersensitivity pneumonitis.

Source control—that is, stopping smoking—appears to be the only reliably effective means of preventing **environmental tobacco smoke** exposure. There is sufficient evidence to conclude that increased ventilation is *technologically capable* of reducing the indoor concentration of ETS particles and gases, and that particle air-cleaning methods are *technologically capable* of reducing the indoor concentration of ETS particles. However, evidence is lacking on whether interventions designed to encourage the use of the

requisite ventilation and air cleaning methods would be associated with a reduction in asthma development or exacerbation.

Control options for **chemical and particulate pollutants** in indoor environments include source modification (removal, substitution, or emission reduction), ventilation (exhaust or dilution), or pollutant removal (filtration). The various forms of pollutant source modification are usually the most effective. For most gaseous pollutants—NO₂ for example—removal via air cleaning is not presently practical.

No intervention studies clearly document that any form of **dampness** control works effectively to reduce symptoms or to reduce the chances of asthma development. However, given its relationship to factors (such as dust mites and fungal growth) associated with asthma, steps to reduce dampness may be appropriate. For homes, these measures include powered mechanical ventilation to remove or dilute occupant-generated moisture, proper installation of vapor barriers, channeling ground water away from foundations, sealing below-ground walls to prevent water intrusion, protecting ground-level concrete slabs from moisture intrusion, and constructing crawl spaces to prevent water intrusion.

There are both theoretical evidence and limited empirical data indicating that feasible modifications in **ventilation** rates can decrease or increase⁴ concentrations of some of the indoor pollutants associated with asthma by up to approximately 75%. Limited or suggestive evidence exists to indicate that particle **air cleaning** is associated with a reduction in the exacerbation of asthma symptoms. Theoretical and limited empirical data indicate that particle air cleaners are most likely to be effective in reducing the exacerbation of asthma symptoms associated with particles smaller than approximately 2 μm, such as ETS particles⁵ and some airborne cat allergen. There is insufficient evidence to determine whether or not the use of particle air cleaners is associ-

⁴The indoor concentrations of some pollutants from outdoors—particulate matter and ozone, for example—may increase with the ventilation rate.

⁵Particle air cleaners are *not* effective in reducing concentrations of the gaseous components of ETS.

ated with decreased asthma development. It should also be noted that microorganisms can grow on some air-cleaning equipment such as filter media; thus, improperly maintained air cleaners are also a potential source of indoor pollutants.

Inadequate or insufficient information was available regarding several other interventions. These are discussed in Chapters 5 through 10.

It is difficult to draw general conclusions regarding effective indoor environmental interventions. However, the committee is able to offer some observations. For many allergens, effective strategies consist of integrated approaches consistently applied over time. The two primary components of an integrated approach are (1) removal or cleaning of allergen reservoirs and (2) control of new sources of exposure. Source removal—where it is possible—is typically the most effective control measure and may be the only effective measure for some agents. Avoidance of exposure through source removal, substitution, or emission reduction is usually the most successful approach for chemical agents.

GENERAL RESEARCH RECOMMENDATIONS AND CONCLUSIONS

Asthma is a complex illness. The many variables that determine its development and severity defy simple summary. Although great strides have been made over the past few years in elucidating mechanisms and understanding the role of environmental and genetic influences, much work remains to be done. Importantly, we still do not know whether or to what extent the reported increases in asthma can be attributed to indoor exposures.

Subsequent chapters of this report contain specific recommendations for further research on the biologic and chemical agents addressed and on the characteristics of indoor environments that may influence asthma outcomes. A digest of these recommendations is contained in Chapter 11. Some general observations are offered below.

The factors that determine the predisposition to sensitivity to certain agents and lead to the development of asthma are still not well understood. There is a great need for studies that rigorously

examine the role of prenatal exposure and whether the age of first exposure influences the development of sensitization. The interaction of different environmental exposures with genetic susceptibilities—a topic of great interest but little research progress—also has to be pursued.

A major problem in choosing and implementing an intervention to mitigate an exposure is the generally limited data available. The limitations exist in regard to both the quantity and the quality of research data. Many of the studies reported are not based on rigorous protocols. Definition of clinical outcome (especially in infants), measurement of exposure, rigorous study design, appropriate population selection, and generalizability of the findings are among the issues that are often not adequately addressed. Indoor environments typically include exposures to multiple potentially problematic agents—dust mites and fungi, for example, are ubiquitous. It has proven difficult to assess the individual roles of the factors implicated in existing studies because complete characterization of exposures has not been done. Therefore, it is often not possible to determine with confidence whether any effects noted are indeed the results of specific exposures studied or of confounders.

The poor and inner city residents are vulnerable populations for asthma development, morbidity, and mortality. As such, there is great interest in identifying effective means to address prevalent exposure problems. Although some research on interventions has been directed at these populations, some of the strategies tried may not be practical to implement unless the subjects are part of an organized protocol providing guidance and funds. Further, individuals living in public or rental housing, or in multifamily units, may not have control over parts of their indoor environment that would be desirable to modify, such as carpeting, excessive moisture, and comprehensive pest management. Future research has to address more effectively the feasibility and generalizability of intervention programs on target populations.

Finally, to date there has been little connection between the scientific literature regarding asthma and the scientific literature regarding the characteristics of healthy indoor environments (for example, building design and operation; and sources, transport, control methods, and exposures to indoor pollutants). Relatively

little of the existing medical and epidemiologic literature on asthma quantifies indoor environmental conditions such as humidity, ventilation, and pollutant concentrations or exposures in sufficient detail. The effectiveness of exposure limitation strategies in reducing exposures and asthma development or exacerbation has, in general, been inadequately studied. These are areas of research that have the potential to impact public health significantly. The committee believes that better communication between medical, public health, behavioral science, engineering, and building professionals is likely to result in more informed studies on the causes of asthma and the means to limit problematic exposures. The committee encourages efforts to bring these groups together to educate one another on their areas of expertise. Although considerable work has been done and is being done on asthma per se, increased research efforts are needed to address the characteristics of healthy indoor environments. Asthma research clearly needs interdisciplinary involvement—not only of clinicians, immunologists, and researchers in related biologic areas—but also of engineers, architects, materials manufacturers and others who are responsible for the design and function of indoor environments. Collaborations should be fostered, and consideration should be given to formulating model research protocols that include indoor environmental characteristics.

REFERENCES

- Benson V, Marano MA. 1998. Current estimates from the National Health Interview Survey, 1995. National Center for Health Statistics. Vital Health Statistics Series 10 No. 199. DHHS Publication PHS 98-1527.
- Carr W, Zeitel L, Weiss K. 1992. Variations in asthma hospitalizations and deaths in New York City. *American Journal of Public Health* 82:59–65.
- Lang DM, Polansky M. 1994. Patterns of asthma mortality in Philadelphia from 1969 to 1991. *New England Journal of Medicine* 331:1542–1546.
- Mannino DM, Homa DM, Pertowski CA, Ashizawa A, Nixon LL, Johnson CA, Ball LB, Jack E, Kang DS. 1998. Centers for Disease Control and Prevention. Surveillance for Asthma Prevalence—United States, 1960–1995. *Morbidity and Mortality Weekly Report*. 47(No. SS-1):1–28.
- National Academy of Sciences (NAS). 1994. *Science and Judgement in Risk Assessment*. National Academy Press: Washington, DC.
- Rappaport S, Boodram B. 1998. Forecasted state-specific estimates of self-reported asthma prevalence—United States, 1998. *Morbidity and Mortality Weekly Report* 47(47):1022–1025.

CLEARING THE *Air*

ASTHMA AND
INDOOR AIR EXPOSURES

Committee on the Assessment of
Asthma and Indoor Air

Division of Health Promotion and
Disease Prevention

INSTITUTE OF MEDICINE

NATIONAL ACADEMY PRESS
Washington, D.C.

NATIONAL ACADEMY PRESS • 2101 Constitution Avenue, N.W. • Washington, D.C. 20418

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competences and with regard for appropriate balance.

Support for this study was provided by the U.S. Environmental Protection Agency (contract no. X825863-01-3). The views presented in the book are those of the Institute of Medicine Committee on the Assessment of Asthma and Indoor Air and are not necessarily those of the funding organization.

Library of Congress Cataloging-in-Publication Data

Institute of Medicine (U.S.). Committee on the Assessment of Asthma and Indoor Air. *Clearing the air : asthma and indoor air exposures* / Committee on the Assessment of Asthma and Indoor Air, Division of Health Promotion and Disease Prevention, Institute of Medicine.
p. cm.

Includes bibliographical references and index.

ISBN 0-309-06496-1 (case)

1. Asthma. 2. Indoor air pollution. 3. Asthma—Government policy—United States. I. Title.

RA645.A83 I55 2000

362.1'96238—dc21

00-025801

Clearing the Air: Asthma and Indoor Air Exposures is available for sale from the National Academy Press, 2101 Constitution Avenue, N.W., Box 285, Washington, DC 20055. Call 800-624-6242 (202-334-3313 in the Washington DC metropolitan area) or visit the NAP's on-line bookstore at www.nap.edu.

For more information about the Institute of Medicine, visit the IOM home page at www.iom.edu.

Copyright 2000 by the National Academy of Sciences. All rights reserved.

Printed in the United States of America.

The serpent has been a symbol of long life, healing, and knowledge among almost all cultures and religions since the beginning of recorded history. The image adopted as a logotype by the Institute of Medicine is based on a relief carving from ancient Greece, now held by the Staatliche Museen in Berlin.

THE NATIONAL ACADEMIES

National Academy of Sciences
National Academy of Engineering
Institute of Medicine
National Research Council

The **National Academy of Sciences** is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Dr. Bruce M. Alberts is president of the National Academy of Sciences.

The **National Academy of Engineering** was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Dr. William A. Wulf is president of the National Academy of Engineering.

The **Institute of Medicine** was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Dr. Kenneth I. Shine is president of the Institute of Medicine.

The **National Research Council** was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Dr. Bruce M. Alberts and Dr. William A. Wulf are chairman and vice chairman, respectively, of the National Research Council.

COMMITTEE ON THE ASSESSMENT OF ASTHMA AND INDOOR AIR

RICHARD B. JOHNSTON, Jr., M.D. (*Chair*), Professor,
Department of Pediatrics, University of Colorado School of
Medicine, and National Jewish Medical and Research
Center, Denver

HARRIET A. BURGE, Ph.D., Associate Professor of
Environmental Health, Department of Environmental
Health, Harvard School of Public Health

WILLIAM J. FISK, M.S., P.E., Staff Scientist/Group Leader,
Indoor Environment Department, Lawrence Berkeley
National Laboratory, Berkeley, California

DIANE R. GOLD, M.D., M.P.H., Assistant Professor of
Medicine, Harvard Medical School, and Assistant Professor,
Environmental Health, Harvard School of Public Health

LEON GORDIS, M.D., Dr.P.H., Professor of Epidemiology,
School of Hygiene and Public Health, The Johns Hopkins
University

MICHAEL M. GRUNSTEIN, M.D., Ph.D., Professor,
Department of Pediatrics, Children's Hospital of
Philadelphia

PATRICK L. KINNEY, Sc.D., Associate Professor, Division of
Environmental Health Sciences, Columbia School of Public
Health

HERMAN E. MITCHELL, Ph.D., Adjunct Professor of
Biostatistics, University of North Carolina, School of Public
Health, Senior Research Scientist, Rho Federal Systems
Division, Chapel Hill, North Carolina

DENNIS R. OWNBY, M.D., Professor of Pediatrics, Medical
College of Georgia

THOMAS A. E. PLATTS-MILLS, M.D., Ph.D., Professor,
Department of Medicine and Microbiology, and Chief,
Division of Allergy, Asthma, and Clinical Immunology,
University of Virginia Health Sciences Center

SAMPSON B. SARPONG, M.B.Ch.B., Assistant Professor of
Pediatrics, The University of Chicago Children's Hospital

SANDRA WILSON, Ph.D., Senior Staff Scientist and Chair,
Department of Health Services Research, Palo Alto Medical
Foundation, Palo Alto, California

Staff

DAVID A. BUTLER, Study Director

JAMES A. BOWERS, Research Assistant

JENNIFER A. COHEN, Research Assistant

ROSE MARIE MARTINEZ, Director, Division of Health
Promotion and Disease Prevention (as of December 1999)

KATHLEEN R. STRATTON, Director, Division of Health
Promotion and Disease Prevention (through November
1999)

DONNA D. DUNCAN, Division Assistant

ANDREA COHEN, Financial Associate

PREFACE

The tremendous burden of disease imparted by asthma, the alarming escalation of asthma prevalence, and the doubling of the asthma mortality rate in the United States since the 1970s have attracted increased attention from those concerned about the health of the American public, including Congress. Many agencies of the U.S. government have been charged to increase their efforts at addressing at least one facet of the problem, from research into pathogenesis by the National Institutes of Health to examination of environmental factors by the Environmental Protection Agency (EPA). It is highly likely that such a rapid rise in asthma prevalence is due to a change in some factor or factors in the environment. Identifying these factors could allow remediation, and—perhaps—prevention. Within this context the EPA sought the guidance of the Institute of Medicine (IOM) in evaluating the quality and nature of the scientific data relating constituents of indoor air and the occurrence of asthma.

The multidisciplinary committee convened by the IOM to respond to this charge, with considerable help from IOM staff, spent many hours in literature review and discussion. Our goal was to reach consensus about how strongly the research data implicated various components of indoor air as causes of asthma. A second goal was to evaluate the state of the scientific evidence concerning specific strategies for exposure mitigation and prevention.

Common problems frustrated our efforts, starting with the imprecise and variable definition of asthma used in research studies, and followed immediately by what it means to “cause” asthma. An unfortunate configuration of genes that influence the immune or inflammatory responses might be said to be the primary “cause” of asthma. But even identical twins may differ as to whether they have asthma or not. Exposure to some environmental factor or factors is required to elicit the clinical expression of asthma, i.e., cause the *development* of asthma. The same or other agents may then cause *exacerbation* of asthma symptoms in these individuals. Thus, the committee divided its analysis into whether an agent might cause asthma development or exacerbation of symptoms.

Considering how the indoor environment might be modified to reduce the risk of asthma development or exacerbation presented a particularly formidable challenge. It has been known for a long time that changing the environment of an asthmatic individual can reduce symptoms, at least temporarily. Mitigation is possible for individual patients. However, little data are available to allow firm conclusions about specific mitigation techniques applied as a public health measure. Although interventions that might reduce the severity of asthma in individual patients emerge from the committee’s review, it is hard to escape the overwhelming conclusion that more research is desperately needed to form the basis for public health interventions. Too much ignorance remains regarding the biologic changes that permit the disease to emerge and recur, the environmental “causes” that may underlie the increased prevalence, the socioeconomic differences in rates of morbidity and mortality, and the means of effective exposure mitigation and prevention. Although it will be essential to gain a better understanding of the relationship between particular agents and asthma, no single agent or factor has yet been identified as a necessary or sufficient cause of asthma. Until a more fundamental understanding is available, multifaceted approaches will be needed to address the interrelationships among biologic, environmental, and socioeconomic factors that permit expression of this disease.

The committee exercised final responsibility for all content of the report, but we were not its only contributors. In fact, we could

not have completed our task satisfactorily without the substantial help of the individuals cited in the Acknowledgments section. We are especially indebted to Peter J. Gergen, Donald K. Milton, William B. Rose, and Kathleen Kreiss, who furnished text and discussions that were essential to our deliberations on certain subjects. The committee has also recognized that the report could never have been developed without the work of the extraordinary staff assigned to us by the Institute of Medicine—David Butler, James Bowers, Jennifer Cohen, Donna Duncan, Andrea Cohen, and Kathleen Stratton. In particular, David Butler, Study Director, with intelligence, patience, persistence, and hard work, expedited and channeled our deliberations through a dismaying array of subjects, from exposure assessment to pathophysiology, to their final expression as the report.

Richard B. Johnston, Jr., M.D.
Chair

ACKNOWLEDGMENTS

Preparation of this report could not have happened without the guidance and expertise of numerous individuals. Although it is not possible to mention by name all of those who contributed to this committee's work, the committee wants to express its gratitude to a number of individuals for their special contributions.

Sincere thanks go to all of the participants at the workshops convened on January 18 and March 22, 1999. The intent of these workshops was to gather information regarding exposure to specific indoor air allergens and irritants, and asthma pathogenesis, the triggering of asthma attacks, and the exacerbation of symptoms in asthmatics. The speakers, who are listed in Appendix B, gave generously of their time and expertise to help inform and guide the committee's work.

We are particularly appreciative of the efforts of four individuals who contributed text that was used or formed the basis of discussions in this report: Peter J. Gergen, M.D., M.P.H.; Kathleen Kreiss, M.D.; Donald Milton, M.D., Dr.P.H.; and William B. Rose, M.Arch. Their contributions greatly aided the committee and had a significant positive impact. The Committee on the Assessment of Asthma and Indoor Air has, of course, final responsibility for all content in the report.

The committee extends special thanks to the dedicated and hard working staff at the Institute of Medicine (IOM). The exper-

tise and leadership of Kathleen Stratton, Director of the Division of Health Promotion and Disease Prevention, helped to ensure that this report met the highest standards for quality.

This report has been reviewed in draft form by individuals chosen for their diverse perspectives and technical expertise, in accordance with procedures approved by the NRC's Report Review Committee. The purpose of this independent review is to provide candid and critical comments that will assist the institution in making the published report as sound as possible and to ensure that the report meets institutional standards for objectivity, evidence, and responsiveness to the study charge. The review comments and draft manuscript remain confidential to protect the integrity of the deliberative process. We wish to thank the following individuals for their participation in the review of this report: Eula Bingham, University of Cincinnati; Noreen Clark, University of Michigan School of Public Health; Peyton Eggleston, Johns Hopkins University School of Medicine; Leslie Grammer, Northwestern University Medical School; Jonathan Samet, Johns Hopkins University School of Hygiene and Public Health; Olli Seppänen, Helsinki University of Technology; and Scott Weiss, Harvard University School of Medicine. While the individuals listed above have provided constructive comments and suggestions, it must be emphasized that responsibility for the final content of this report rests entirely with the authoring committee and the institution.

Finally, the committee would like to thank the chair, Richard Johnston, Jr., M.D., for his outstanding work, leadership, and dedication to this project.

CONTENTS

EXECUTIVE SUMMARY	1
Organization and Framework, 2	
Conclusions about the Relationship between Indoor Exposures and Asthma, 4	
General Research Recommendations and Conclusions, 16	
1 MAJOR ISSUES IN UNDERSTANDING ASTHMA	19
Origin of the Study, 19	
Summary of the <i>Indoor Allergens</i> Report, 20	
Definitions of Asthma, 22	
Clinical Presentation of Asthma, 24	
Risk Factors for Asthma, 28	
Trends in the Prevalence of Asthma, 29	
Mechanisms of Asthma, 31	
Evaluating the Effectiveness of Interventions to Reduce Asthma, 33	
2 METHODOLOGICAL CONSIDERATIONS IN EVALUATING THE EVIDENCE	39
Evaluating the Evidence, 40	
Summarizing Conclusions Regarding the Evidence, 48	
Assessing Exposures to Agents in Indoor Air, 51	
Other Considerations, 62	

3	PATTERNS OF ASTHMA MORBIDITY AND MORTALITY	67
	The Burden of Asthma, 67	
	Mortality, 68	
	Utilization of Health Care Services, 69	
	Prevalence, 70	
	Severity, 75	
	Trends in Risk Factors, 77	
	Twin, Adoption, and Migrant Studies, 78	
	Socioeconomic Status Versus Race or Ethnicity, 79	
	Asthma Rates in Germany—A Natural Experiment, 80	
	Reflections on the Trends, 81	
4	PATHOPHYSIOLOGICAL BASIS OF ASTHMA	87
	Airway Inflammation in Asthma, 88	
	The Airway Smooth Muscle in Asthma, 96	
	The Genetics of Asthma, 98	
	Conclusion, 99	
5	INDOOR BIOLOGIC EXPOSURES	105
	Animals, 106	
	Cockroach, 124	
	House Dust Mites, 136	
	Endotoxins, 150	
	Fungi, 158	
	Infectious Agents, 175	
	Houseplants, 184	
	Pollen, 186	
6	INDOOR CHEMICAL EXPOSURES	223
	Nitrogen Dioxide, 224	
	Pesticides, 234	
	Volatile Organic Compounds, 237	
	Formaldehyde, 243	
	Fragrances, 247	
	Plasticizers, 250	
	Other Chemical Exposures in the Indoor Environment, 251	

CONTENTS

xv

- 7 EXPOSURE TO ENVIRONMENTAL TOBACCO SMOKE 263
Definition of Environmental Tobacco Smoke (ETS), 264
Factors Controlling Exposure to ETS, 265
Evidence of a Relationship between ETS and Asthma, 271
Conclusions Regarding the Health Impacts of ETS with Respect to Asthma, 280
Evidence Regarding Means of Source Mitigation or Prevention, 281
Conclusions Regarding ETS Source Control or Mitigation: Feasibility and Benefits, 288
Research Needs, 290
- 8 INDOOR DAMPNES AND ASTHMA 298
Indoor Water Sources and Removal Processes, 299
Indoor Dampness and Respiratory Disease, 307
Dampness Control, 310
Research Needs, 311
- 9 ASTHMA AND NONRESIDENTIAL INDOOR ENVIRONMENTS 316
Building-Related Asthma, 316
Studies of Schools, 321
Conclusion, 324
Research Needs, 324
- 10 IMPACT OF VENTILATION AND AIR CLEANING ON ASTHMA 327
Theoretical Background, 327
Building Ventilation, 331
Particle Air Cleaning: Introduction and Review of Conventional Practice, 360
- 11 SUMMARY OF RESEARCH RECOMMENDATIONS AND OVERALL CONCLUSIONS 394
Pathophysiologic Basis of Asthma, 394
Animal Allergens, 394
Cockroach, 396
House Dust Mites, 396

Endotoxin, 397	
Fungi, 398	
Infectious Agents, 398	
Plants, 399	
Nitrogen Dioxide (NO ₂), 399	
Pesticides, 399	
Plasticizers, 400	
Volatile Organic Compounds, 400	
Fragrances, 400	
Environmental Tobacco Smoke (ETS), 401	
Indoor Dampness, Moisture Problems and Moisture Control, 402	
Nonresidential Indoor Environments, 402	
Ventilation, 403	
Air Cleaning, 404	
Overall Conclusions, 405	
APPENDIXES	
A Theoretical Considerations Relevant to the Influence of Ventilation and Air Cleaning on Exposures to Indoor-Generated Pollutants	409
B Workshop Summaries	415
C Committee and Staff Biographies	418
INDEX	425

CLEARING THE *Air*

