Asthma in the United States: Burden and Current Theories

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Asthma has emerged as a major public health problem in the United States over the past 20 years. Currently, nearly 15 million Americans have asthma, including almost 5 million children. The number of asthma cases has more than doubled since 1980. Approximately 5,500 persons die from asthma each year, and rates have increased over the past 20 years. Rates of death, hospitalization, and emergency department visits are 2–3 times higher among African Americans than among white Americans. The costs of asthma have also increased to $12.7 billion in 1998. Both lifestyle and environmental hypotheses have been invoked to explain the increase in asthma prevalence. Several studies have examined the relationship of obesity and asthma and found associations suggesting that obesity predisposes to the development of asthma. Some studies have found that day care attendance and having older siblings protect against the development of asthma. This observation has led investigators to hypothesize that increased exposure to microbial agents might protect against asthma (the hygiene hypothesis). Environmental exposures found to predispose to asthma include house dust mite allergen and environmental tobacco smoke. Although current knowledge does not permit definitive conclusions about the causes of asthma onset, better adherence to current recommendations for medical therapy and environmental management of asthma would reduce the burden of this disease. ***Key words:*** **asthma, epidemiology, hygiene, incidence, indoor environment, obesity.** ***Environ Health Perspect*** **110(suppl 4):557–560 (2002).**
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Epidemiology and Economic Impact of Asthma

Asthma has emerged as a major public health problem in the United States over the past 20 years. This overview of the epidemiology of asthma in the United States *a*) reviews what we know about asthma in the United States, including its cost; *b*) describes several current theories that might explain the phenomenon we are experiencing; and *c*) discusses what we should be doing to control this modern epidemic of a chronic and environmental disease.

The striking fact is that asthma is much more common than it was 20 years ago. The number of persons with self-reported asthma has more than doubled between 1980 and 1996 (Figure 1), with the greatest increase in the prevalence rate among children of preschool age (*1*). Although the diagnosis of asthma is more difficult among young children (and potentially confounded by comorbid conditions in older persons), the magnitude of the increase suggests that it is not due solely to changes in diagnostic practices or changes in coding practices. Work from Olmstead County, Minnesota, documented an increasing asthma incidence rate from 1964 to 1983 among children (*2*). National data show increases in prevalence in all age, race, and ethnic groups and among both males and females. Data from a recent survey that collected information only on adults suggest that this trend has continued; the estimated number of adults with asthma has reached 14.6 million persons, 7.2% of the U.S. population (*3*).

As the number of cases of asthma was increasing, so was the number of persons dying from asthma (Figure 2) (*1*). Most deaths due to asthma occurred in adults over 35 years of age, especially among adults over 65 years of age. This increase dates from the mid-1970s, when deaths from asthma reached a nadir. The rate of hospitalization for asthma increased during the late 1980s and has since plateaued. However, the rate among African Americans remained 2–3 times higher than for white Americans (Figure 3). Similar disparate outcomes also exist between white American and African Americans for the rates of death and of emergency department visits. Hispanic Americans in the Northeast also have an elevated risk for death compared with white Americans (*4*). This disparity in outcomes defines one of the key research themes that must be addressed to improve the national picture for asthma.

In addition to better understanding disparities among different race and ethnic groups, we need better surveillance data, specifically data that are more timely and geographically appropriate. Such data will facilitate planning and evaluation of local interventions. With the exception of mortality data and data from the Behavioral Risk Factor Surveillance System (*3*), data are available at regional or national levels only. In addition prevalence rates in the published literature vary widely. It is generally not possible to determine the reasons for this range, although a number of definitions of asthma have been used (including having the symptoms of asthma rather than having physician-diagnosed asthma and ever having been diagnosed with asthma as opposed to currently having asthma), and surveys have been conducted of specific populations at higher risk for asthma than the general population. Surveillance for incident cases of asthma is needed for investigators to better understand why prevalence is increasing. Identifying the characteristics of incident cases would also facilitate studies of the risk factors for the onset of asthma.

The economic costs of asthma to the nation are substantial. Weiss et al. estimated the direct and indirect costs to be $6.2 billion during 1990 (*5*). In 2000, these estimates were updated and different sources of cost were compared with those from the earlier period (*6*). Overall, costs increased approximately 50%. Hospital and emergency department costs had declined and costs for pharmaceuticals had increased. This report (*6*) examined differences in prescribing patterns in the two time periods found that short-acting beta agonists—rescue medications used for the immediate relief of symptoms—had increased to a much greater extent than had the anti-inflammatory agents—medications used to prevent symptoms in persons with persistent asthma. Data from these studies indicated that the estimated cost of asthma rose slightly from 1.16% of direct medical expenses in 1985 to 1.48% in 1994.

Theories on the Origins of the Asthma Epidemic

Asthma has emerged as a substantial problem in the United States. Inexpensive, easy-to-implement interventions to prevent the onset of asthma have not been defined despite some research on the effectiveness of allergen avoidance measures (*7,8*). In fact despite a substantial research effort, the exact causes of nonoccupational asthma are poorly defined. Such definition is a vital prerequisite to establishing and implementing public health approaches to prevent asthma onset. Currently, investigators have proposed several

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theories to explain the increase in asthma prevalance. Below, I briefly review research that points to two lifestyle or behavioral risk factors. I then provide an overview of a review of the role that indoor exposures may play in contributing to the asthma epidemic.

Potential Lifestyle or Behavioral Risk Factors for Asthma for Asthma Onset

The first hypothesis to explain the increasing prevalence of asthma begins with the observation that an increasing proportion of the U.S. population is overweight or obese and that this trend parallels the increasing prevalence rate of asthma (*9*). Several investigators suggest that these similarly increasing trends are more than coincidental, and some evidence has been collected to suggest a relationship between obesity and reduced lung function or asthma (*10–12*). In one of the first prospective studies, Camargo et al. (*10*) examined data from the Nurses' Health Study. Incident asthma was identified from among 85,911 adult female nurses over a 4-year period. Follow-up questionnaires were sent to individuals who may have had new-onset asthma during the observation period to collect additional information on the details of the onset of disease. Three levels of certainty of new-onset asthma were constructed and examined as the outcomes for a variety of risk factors, including body mass index (calculated as weight in kilograms divided by height in meters squared—all collected by questionnaire). A total of 1,596 new-onset asthma cases were identified, an annual incidence rate of 0.5%. The authors found a dose–response effect for body mass indices above 20, with progressively greater risk for new-onset asthma with increasing body mass index. In addition, the risk was progressively greater for each level of specificity of the case definition of new-onset asthma, with the strictest definition having the greatest risk. The authors also had information on physical activity and found similar trends for increasing risk of asthma with decreasing levels of physical activity. Further study is needed to verify these findings in other populations, including men and children, and to determine the effectiveness of weight loss as an intervention to reduce the risk of developing asthma.

The second hypothesis has become known popularly as the "hygiene hypothesis." Several studies have shown that having older or a greater number of siblings protects a child from developing asthma (*13,14*). This protection against developing asthma might be, in part, the result of exposure to infections acquired from older siblings. The study that I describe here in more detail was conducted in Tucson, Arizona (*15*), and examined the risk for developing asthma in a cohort of children born between 1980 and 1984. Information about the onset of asthma and about two cardinal symptoms of asthma—wheezing and whistling in the chest—was collected with a standard questionnaire. Risk factors for asthma onset included the number of older siblings and their ages at the time of enrollment in day care. Children with older siblings were at lower risk for asthma at 11 and 13 years of age. Enrollment of infants 0–4 months of age in day care likewise was associated with a reduced risk of asthma at 11 and 13 years of age compared with enrollment at older ages or not attending day care. Asthma symptoms at 2 years of age were more likely among children with older siblings or early attendance in day care but less likely at 11 and 13 years of age.

These results suggest that asthmalike symptoms in early childhood could be caused by infection; experience with infection early in life could then result in reduced subsequent risk for allergic asthma (*16*). This immunological explanation has some basis in what is known about the development of the immune system in early life. The T-helper (T_H) cell line of lymphocytes has two distinct components: T_H1, which mediates cell-mediated immunity and is a mature manifestation of immune function, and T_H2, which mediates antibody production (*16*). At the time of birth, T_H lymphocytes are largely T_H2; over time a T_H1 type of immune response develops. According to the hygiene hypothesis, modern life with reduced risk of infection is associated with a skewing of the population toward T_H2-type immune responses. T_H1 and T_H2 are defined in a practical sense by measuring the production of various cytokines, with specific cytokines being associated with T_H1 or T_H2 immune responses. These data do not yet provide a definitive conclusion on whether improved hygiene has caused the increase in asthma prevalence (*17,18*).

Environmental Exposures and Asthma Onset

In addition to the overweight/physical activity hypothesis and the hygiene hypothesis, many investigators have sought to identify specific environmental exposures associated with the development of asthma. With the exception of specific work-related exposures (*19*), this effort has not produced a unifying theory or set of observations to explain the asthma epidemic. The U.S. Environmental Protection Agency commissioned the Institute of Medicine to review

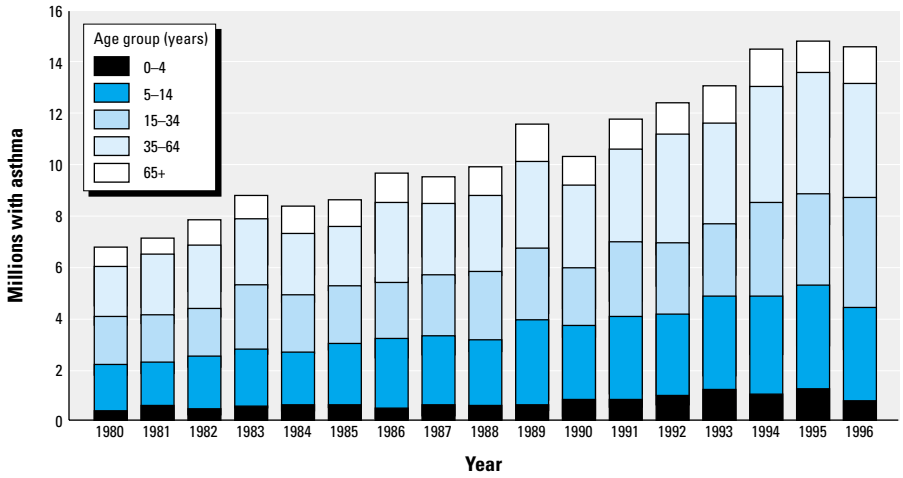

Figure 1. Number of people with asthma, United States, 1980–1996.

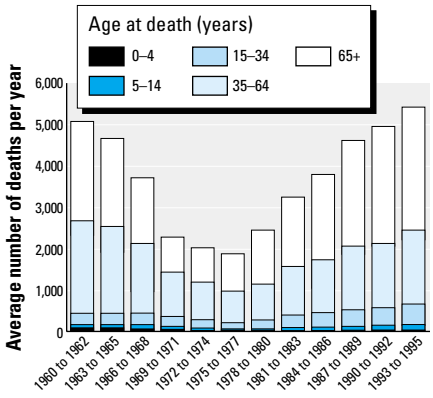

Figure 2. Deaths due to asthma, United States, 1960–1995.

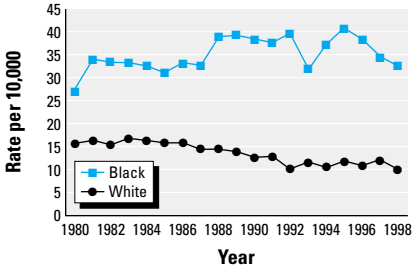

Figure 3. Rate of hospitalization due to asthma, United States, 1980–1998.

the available evidence for relationships between indoor environmental exposures and asthma to make recommendations for mitigating these exposures on the basis of the scientific literature and to suggest areas for future research. In 2000, the Institute of Medicine published a report based on this review. The review is comprehensive and is concerned with both exposures that may be related to onset of asthma and factors related to worsening of already established asthma (*20*). An elaborate classification scheme was used to evaluate each exposure; the evidence was categorized as follows: *a*) exposures with evidence of a causal relationship, *b*) exposures with evidence of an association, *c*) exposures with limited or suggestive evidence, *d*) exposures with inadequate evidence, and *e*) exposures with limited or suggestive evidence of no association.

For biological exposures related to the development of asthma, exposure to house dust mite allergen was classified as having evidence of a causal relationship. Exposure to cockroach allergen and exposure to respiratory syncytial virus were classified as having limited or suggestive evidence. Exposure to rhinovirus among adults was classified as having limited or suggestive evidence of no association. Inadequate or insufficient evidence was found of an association of exposure of mold and asthma onset. For chemical exposures, exposure to environmental tobacco smoke among children of preschool age had evidence of an association. All other exposures were classified as having inadequate evidence.

This lengthy review (*20*), from which only the conclusions have been cited, also included suggestions for future research. The committe at the Institute of Medicine recommended an emphasis on examining exposures early in life, including prenatal exposures, and on attempting to define the age at first exposure to substances that could be related to the onset of asthma. The committee stressed the need for improved understanding of gene–environment interactions. In addition, the committee suggested the need to examine exposure reduction strategies and to include rigorous mitigation trials. Ultimately, better integration of the health sciences and healthy environment sciences is needed to achieve these research aims.

Up to this point I have concentrated on indoor environmental exposures. Ambient or outdoor environmental exposures to ozone and particulate matter (as well as sulfur dioxide and nitrogen oxides) are well-documented causes of asthma exacerbations (*21*). Data on emergency department visits, hospitalizations, and symptoms have shown clear associations with both of these pollutants (*21,22*). What is much less clear is whether ambient outdoor pollution is associated with asthma onset. At a gross level, air pollution levels are lower than they were in the past, yet asthma prevalence has risen substantially over the past 20 years (*23*). This conclusion ignores the differences in changes in air pollution: a sharp reduction for ambient lead but hardly any change in ozone levels. It also overlooks the lack of information on asthma onset and the paucity of studies that have examined exposure to specific pollutants as risk factors for asthma onset. It is likely that such information will be available within the next several years. One study that will have the ability to assess such associations is being conducted in 12 southern California communities (*24*). A recent analysis showed that children who played three team sports and lived in communities with higher ambient ozone concentrations were at increased risk for developing asthma compared with children who lived in communities with lower ozone concentrations or who played fewer team sports (*25*). Although this report should not be interpreted as the final word on the risk of outdoor air pollution for asthma onset, it does demonstrate the type of analysis needed to assess the risk of ambient outdoor exposures for asthma onset.

Summary and Conclusions

In this brief review of asthma epidemiology in the United States, I have highlighted trends in the increasing number of cases, increases in the number of deaths, and the racial and ethnic disparities in the more severe outcomes of asthma. Several theories have been proposed to explain the increased number of cases, but evidence is inadequate to fully explain the phenomenon that has occurred in the United States over the past 20 years. Two indoor environmental exposures—exposure to house dust mites and to environmental tobacco smoke among children of preschool age—have been shown to cause or be associated with asthma onset. Although outdoor ambient environmental exposures are known to cause asthma exacerbations, very limited evidence is available to suggest that these exposures can actually cause the disease itself. Future work may provide more definitive conclusions.

Public health efforts need to be based on current knowledge. Established guidelines for the environmental and medical management of asthma (*26*) are not being followed (*27,28*). If they were followed, a substantial reduction in morbidity and mortality would be expected. Improved implementation of these consensus guidelines as well as intensified efforts to track the prevalence, severity, and quality of asthma management is needed to reduce the needless burden of asthma.

References and Notes

1. Mannino DM, Homa DM, Pertowski CA, Ashizawa A, Nixon LL, Johnson CA, Ball LB, Jack E, Kang DS. Surveillance for asthma—United States, 1960-1995. Morb Mortal Wkly Rep 47(SS-1):1–27 (1998).
2. Yunginger JW, Reed CE, O'Connell EJ, Melton LJ III, O'Fallon WM, Silverstein MD. A community-based study of the epidemiology of asthma. Incidence rates, 1964-1983. Am Rev Respir Dis 146:888–894 (1992).
3. Centers for Disease Control and Prevention. Self reported asthma prevalence among adults, United States, 2000. Morb Mortal Wkly Rep 50:682–686 (2001).
4. Homa DM, Mannino DM, Lara M. Asthma mortality in U.S. Hispanics of Mexican, Puerto Rican, and Cuban heritage, 1990-1995. Am J Respir Crit Care Med 161:504–509 (2000).
5. Weiss KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States. N Engl J Med 326:862–826 (1992).
6. Weiss KB, Sullivan SD, Lyttle CS. Trends in the cost of illness for asthma in the United States, 1985-1994. J Allergy Clin Immunol 106:493–499 (2000).
7. Hide DW, Matthews S, Matthews L, Stevens M, Ridout S, Twisleton R, Gant C, Arshad SH. Effect of allergen avoidance in infancy on allergic manifestation at age two years. J Allergy Clin Immunol 93:842–846 (1994).
8. Custovic A, Simpson BM, Simpson A, Kissen P, Woodcock AK. Effect of environmental manipulation in pregnancy and early life on respiratory symptoms and atopy during first year of life: a randomised trial. Lancet 358:188–193 (2001).
9. Mokdad A, Serdula M, Dietz W, Bowman B, Marks J, Koplan J. The spread of the obesity epidemic in the US. JAMA 282:1519–1522 (1999).
10. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Arch Intern Med 159:2582–2588 (1999).
11. Shaheen SO, Sterne JA, Montgomery SM, Azima H. Birth weight, body mass index and asthma in young adults. Thorax 54:396–402 (1999).
12. Chen Y, Horne SL, Dosman JA. Body weight and weight gain related to pulmonary function decline in adults: a six year follow up study. Thorax 48:375–380 (1993).
13. Rona RJ, Dduran-Tauleria E, Chinn S. Family size, atopic disorders in children, and ethnicity. J Allergy Clin Immunol 99:454–460 (1997).
14 Bodner C, Godden D, Seaton A. Family size, childhood infections and atopic diseases. The Aberdeen WHEASE Group. Thorax 53:28–32 (1998).
15. Ball TM, Castro-Rodriguez JA, Griffith KA, Holberg CJ, Martinez FD, Wright AL. Siblings, day-care attendance, and the risk of asthma and wheezing during childhood. N Engl J Med 343:538–543 (2000).
16. Busse WW, Lemanske RF. Asthma. N Engl J Med 344:350–362 (2001).
17. Platts-Mills TA, Woodfolk JA, Sporik RB. Con: the increase in asthma cannot be ascribed to cleanliness. Am J Respir Crit Care Med 164:1106–1107 (2001).
18. Salvi SS, Babu KS, Holgate ST. Is asthma really due to a polarized T cell response toward a helper T cell type 2 phenotype? Am J Respir Crit Care Med 164:1343–1346 (2001).
19 Bernstein DI. Allergic reactions to workplace allergens. JAMA 278:1907–1913 (1997).
20. IOM. Committee on the Assessment of Asthma and Indoor Air, Division of Health Promotion and Disease Prevention, Institute of Medicine. Clearing the Air: Asthma and Indoor Air Exposures. Washington, DC:National Academy Press, 2000.
21. Linn WS, Gong H Jr. The 21st century environment and air quality influences on asthma. Curr Opin Pulm Med 5:21–26 (1999).
22. Tolbert PE, Mulholland JA, MacIntosh DL, Xu F, Daniels D, Devine OJ, Carlin BP, Klein M, Dorley J, Butler AJ, et al. Air quality and pediatric emergency room visits for asthma in Atlanta, Georgia, USA. Am J Epidemiol 151:798–810 (2000).
23. U.S. EPA. National Air Quality and Emissions Trends Report, 1999. EPA 454/R-01-004. Research Triangle Park, NC:U.S. Environmental Protection Agency, 2001.
24. Peters JM, Avol E, Navidi W, London SJ, Gauderman WJ, Lurmann F, Linn WS, Margolis H, Rappaport E, Gong H, et al.

A study of twelve southern California communities with differing levels and types of air pollution. I: Prevalence of respiratory morbidity. Am J Respir Crit Care Med 159:760–767 (1997).

25. McConnell R, Berhane K, Gilliland F, London SJ, Islam T, Gauderman WJ, Avol E, Margolis HG, Peters JM. Asthma in exercising children exposed to ozone: a cohort study. Lancet 359:386–391 (2002).
26. National Asthma Education and Prevention Program (NAEPP). Expert Panel Report 2: Guidelines for the Diagnosis and Management of Asthma. NIH Publ no. 97-4051.Bethesda, MD:National Heart, Lung, and Blood Institute, 1997.
27. Jatulis DE, Meng YY, Elashoff RM, Schocket AL, Evans RM, Hasan AG, Legorreta AP. Preventive pharmacologic therapy among asthmatics: five years after publication of guidelines. Ann Allergy Asthma Immunol 81:82–88 (1998).
28. Hartert TV, Windom HH, Peebles RS, Freidhoff LR, Togias A. Inadequate outpatient medical therapy for patients with asthma admitted to two urban hospitals. Am J Med 100:386–394 (2000).