Box 1.9 Why the Increase in Asthma?

Over the past two decades, researchers have reported a startling rise in the prevalence of asthma among children and young adults. This trend persists today, mostly in affluent countries, leading some to call asthma a disease of the industrialized 20th Century (1). Indeed, asthma appears to be rare in developing countries, although some evidence suggests that the disease is emerging in urban centers in parts of Africa and Asia as well (2).

In many affluent countries where asthma is common today, its prevalence has climbed nearly 50 percent in just a 10-year span (3). Rates of hospitalization for asthma are also rising in these countries, a fact that suggests the disease is becoming more severe (4). Particularly disturbing is the rise in the number of deaths attributed to asthma. Asthma deaths among people 5 to 34 years of age increased more than 40 percent between the mid-1970s and mid-1980s in most countries studied (5).

Improved diagnosis and greater awareness of asthma may partly account for the rising number of cases (6). Similarly, changes in health insurance and medical practice may contribute to the rise in hospitalization rates for asthma. Even considering these factors, many researchers are convinced that the increase is real (7). This recognition has prompted a large-scale effort to find out what could be driving the increase. Although a definitive answer remains elusive, environmental factors have emerged as key.

A Hunt for Clues

Asthma is a complex disease whose development is influenced by both host susceptibility and environmental or lifestyle factors (8). Some people are genetically predisposed to develop asthma. Other people acquire asthma, often in early childhood, for reasons that are still unclear but seem to involve early and repeated exposure to a variety of factors in the environment, including allergens and viruses.

People with asthma are exquisitely sensitive to certain external triggers, typically allergens like pollen or cat dander but also viral infections, exercise, cold air, tobacco smoke, and air pollution. When exposed to one of these triggers, someone with a common allergy, such as hay fever, may develop a runny nose or sneezing. For an asthmatic, however, exposure triggers a cascade of events in which certain immune cells marshal other cells that then launch an inflammatory attack on the respiratory system, causing the airways to constrict and making breathing difficult.

Evidence that environmental factors play a major role in prevalence of asthma comes from a number of investigations. First, although genetics clearly influences the development of asthma, studies of twins suggest genetic tendencies might account for 20 to 75 percent of asthma cases, leaving a substantial number unexplained (9)(10). Still other studies show that when people migrate to new areas, their risk of developing asthma often changes (11). Other clues can be discerned from looking at the variable distribution of asthma prevalence across the globe.

Asthma is generally more prevalent in urban areas, although South Australia is an important exception (12). Mortality rates from asthma are also higher in urban areas for some countries (13). In most countries, asthma is most pronounced among the higher socioeconomic classes (14). However, in the United States, poor and minority populations are disproportionately affected. In the United States, increases in asthma prevalence have been found among all groups of children and youths, but they are highest among poor, black, and Hispanic children (15)(16). Poverty and race also appear to be important risk factors in asthma mortality. In the United States in 1993, black children were four times more likely than white children to die from asthma (17). In New York City's East Harlem, the mortality rate is 10 times the national average (18).

Outdoor Air Pollution

Numerous studies have shown that episodes of air pollution can exacerbate existing asthma conditions—by either triggering or worsening an attack (19). Emergency room visits for asthma often increase after a bout of air pollution, as do hospitalizations. However, because air pollution is composed of a mix of pollutants that vary from location to location, it is difficult to tease apart which pollutants are to blame.

The urban pollutant with perhaps the worst record for provoking asthma or exacerbating its symptoms is ozone, a principal component of smog. Low levels of ozone trigger coughing, hampered and painful breathing, and inflammation of the airways in both healthy and asthmatic people (20). Ozone exposure also seems to render people more susceptible to other irritants, either pollutants or allergens such as dust mites (21)(22).

Evidence is conflicting regarding the links between sulfur dioxide and nitrogen oxide and asthma. Recent attention has turned to fine particulate pollution, or PM_{10}. Several studies have linked fine particulate pollution with increased asthma symptoms and emergency room visits (23). But opinion remains divided on whether air pollution is contributing to the increase in asthma prevalence. What confounds some researchers is that many developed countries are showing a rise in the prevalence of asthma, yet an overall decline in air pollution.

Overall, the body of evidence suggests that although air pollution may play a role, it alone is not the driving force behind the increase in asthma prevalence and mortality. Asthma researcher David Bates of the University of British Columbia in Vancouver summarized the situation recently: "We have good reason to be suspicious of the contemporary role of air pollutants, but proof is something else" (24).

Indoor Air Pollution

Asthma in children and young adults is strongly associated with sensitization to allergens found in homes. Tobacco smoke, for one, is known to increase the risk of asthma. Children have about twice the risk of developing asthma if one or both parents are cigarette smokers (25). Beyond tobacco smoke, the chief culprits indoors appear to be microscopic dust mites that inhabit bedding, furniture, and carpets, and also cockroach parts and animal dander. Toxic cleaning agents and pesticides may also be involved, although their role is less clear (26).

Increasingly, attention is focused on bio-allergens such as dust mites and cockroaches. Dust mites have long been known to increase the risk of asthma. Indeed, high exposures to them in infancy seem to lead to early onset of asthma (27). In general, children who become allergic to foreign proteins—such as insect parts or animal dander in the home—have an increased risk of developing asthma, and continued exposure contributes to the disease. Increasing numbers of homes and buildings are now "air tight," which can lock in bio-allergens and also cigarette smoke and other pollutants.

A number of recent changes in the indoor environment—such as carpeting, upholstered furniture, mattresses, humidifiers, and central air conditioning or heating—make it easier for dust mites and molds, another potent allergen, to thrive. For example, one study in Denver, Colorado, found that although the city is located in a dry climate not conducive to dust mites, the air conditioning in homes nonetheless fostered significant dust mite levels (28).

In the United States, some of the strongest evidence to date implicates a well-known urban denizen, the cockroach. Indeed, early and continued exposure to cockroaches appears to shed light upon the disproportionate prevalence of asthma among poor, inner-city children, as studies suggest that the degree to which people are exposed to cockroaches correlates with their socioeconomic status (29).

Evidence from a 1997 study suggests that cockroaches play an even larger role than previously believed (30). This large study of eight urban areas in the United States found that asthma was most pronounced among children

Box 1.9 continued

who are allergic to cockroach allergens and are exposed to a high level of that allergen in bedroom dust. Specifically, those who were allergic to cockroaches and heavily exposed to them at home were 3.4 times more likely to be hospitalized than other poor, asthmatic youth. They also lost more sleep and school days because of asthma problems. Although roughly the same proportion of the youth tested as allergic to both cockroaches and dust mites (roughly 35 percent) and 23 percent were allergic to cat dander, cockroach allergen was far more prevalent in their bedrooms (31).

Exposure to allergens alone is not sufficient to account for increased severity of asthma among poor and minority populations. Social factors are clearly at play, chief among them limited access to appropriate medical care. One study found fewer medications were prescribed to control asthma in adolescents from low-income homes compared to their peers in more affluent homes (32).

Changing Lifestyles

What is more, many people in developed countries are spending an increasing amount of time indoors. In many affluent countries, indoor sources of entertainment, such as computer games, television shows, and videos, are rapidly replacing outdoor playgrounds. This scenario has led several asthma experts to postulate that the rise of the "indoor amusement culture," perhaps coupled with a lack of exercise, may contribute to the increase in asthma seen in developed countries (33).

Numerous changes related to medical practice in the more developed nations, from the availability of asthma medicines to the changing patterns of childhood infections, may also play a role. Overuse of bronchodilator inhalers has been implicated in the rise in asthma mortality in several countries (34). However, as elevated mortality rates among poor populations suggest, undermedication is likely to be a greater problem (35).

Other researchers hypothesize that some of the benefits of modern medicine may in fact be reducing immunologic protection, rendering some people more susceptible to asthma (36). Although viral infections are known to exacerbate asthma, some studies suggest that having certain infections during early childhood can protect a child from later developing the disease, perhaps by stimulating an immune response that suppresses later allergic reactions (37)(38). Similarly, the rise in asthma in developed nations might also be due, in part, to an increase in the number of surviving premature babies, as these infants are more prone to developing asthma (39).

If any consensus exists in the rapidly changing field of asthma research, it is that no single factor is sufficient to explain current trends in asthma. More likely, suggest researchers such as Woolcock and Peat, "a number of lifestyle changes may have combined to cause the disease to be expressed in children who, in previous times, were immunologically protected from developing asthma—or were not exposed to high allergen levels"(40). Sorting out the role of environmental and lifestyle factors will be key in devising strategies to prevent this debilitating disease.

References and Notes

1. Thomas A.E. Platts-Mills and Melody C. Carter, "Asthma and Indoor Exposure to Allergens," *The New England Journal of Medicine*, Vol. 336, No. 19 (May 8, 1997), p. 1384.
2. Ann J. Woolcock and Jennifer K. Peat, "Evidence for the Increase in Asthma Worldwide," in *The Rising Trends in Asthma*, Ciba Foundation Symposium 206 (John Wiley & Sons, Chichester, U.K., 1997), pp. 123–125.
3. Kevin Weiss, Peter Gergen, and Diane Wagener, "Breathing Better or Wheezing Worse? The Changing Epidemiology of Asthma Morbidity and Mortality," *Annual Review of Public Health*, Vol. 14 (1993), pp. 493–494.
4. Richard Beasley, Neil Pearce, and Julian Crane, "International Trends in Asthma Mortality," in *The Rising Trends in Asthma*, Ciba Foundation Symposium 206 (John Wiley & Sons, Chichester, U.K., 1997), p. 147.
5. M.R. Sears, "Worldwide Trends in Asthma Mortality," *Bulletin of the International Union of Tubercule Lung Disease*, Vol. 66 (1991), p. 80.
6. *Op. cit.* 3, pp. 500–501.
7. *Op. cit.* 4, pp. 142–143.
8. Eugene R. Bleecker, Dirkje S. Postma, and Deborah A. Meyers, "Genetic Susceptibility to Asthma in a Changing Environment," in *The Rising Trends in Asthma*, Ciba Foundation Symposium 206 (John Wiley & Sons, Chichester, U.K., 1997), p. 91.
9. M.L. Edfors-Lubs, "Allergy in 7,000 Twin Pairs," *Acta Allergologica*, Vol. 26 (1971), pp. 249–285.
10. Peter Gergen, National Institute of Allergy and Infectious Diseases, national Institutes of Health, Rockville, Maryland, January 14, 1998 (personal communication).
11. C.H. van Niererk *et al.*, "Prevalence of Asthma: A Community Study of Urban and Rural Xhosa," *Clinical Allergy*, Vol. 9 (1979), pp. 319–24, cited in Anthony Newman-Taylor, "Environmental Determinants of Asthma," *Lancet*, Vol. 345 (February 4, 1995), p. 296.
12. Kevin B. Weiss, Peter J. Gergen, and Ellen F. Crain, "Inner-City Asthma: The Epidemiology of an Emerging U.S. Public Health Concern," *Chest*, Vol. 101, No. 6, Supplement (June 1992), p. 362S.
13. Kevin B. Weiss and Diane K. Wagener, "Changing Patterns of Asthma Mortality: Identifying Target Populations at High Risk," *Journal of the American Medical Association*, Vol. 264, No. 13 (October 3, 1990), p. 1687.
14. *Op. cit.* 2, pp. 122–131.
15. Elaine Friebele, "The Attack of Asthma," *Environmental Health Perspectives*, Vol. 104, No. 1 (January 1996), p. 23.
16. Michael Weitzman *et al.* "Recent Trends in Prevalence and Severity of Childhood Asthma," *Journal of the American Medical Association*, Vol. 268, No. 19 (1992), p. 2673.
17. Centers for Disease Control, "Asthma Mortality and Hospitalization Among Children and Young Adults—United States, 1980–1993," *Morbidity and Mortality Weekly Report*, Vol. 45, No. 17 (May 3, 1996), p. 351.
18. *Op. cit.* 12, p. 362S.
19. Hillel S. Koren and Mark J. Utell, "Asthma and the Environment," *Environmental Health Perspectives*, Vol. 105, No. 5 (May 1997), p. 534.
20. Hillel S. Koren, "Associations between Criteria Air Pollutants and Asthma," *Environmental Health Perspectives*, Vol. 103, Supplement 6 (1995), p. 238.
21. David V. Bates, "Observations on Asthma," *Environmental Health Perspectives*, Vol. 103, Supplement 6 (1995), p. 245.
22. Rebecca Bascom, "Environmental Factors and Respiratory Hypersensitivity: The Americas," *Toxicology Letters*, Vol. 86 (1996), pp. 122–124.
23. David V. Bates, "The Effects of Air Pollution on Children," *Environmental Health Perspectives*, Vol. 103, Supplement 6 (1995), p. 50.
24. *Op. cit.* 21, p. 246.
25. National Institutes of Health: Heart, Lung, and Blood Institute (NHLBI), *Global Initiative for Asthma: Global Strategy for Asthma Management and Prevention* (NHLBI/World Health Organization (WHO) Workshop Report, 1995), p. 65.
26. *Op. cit.* 3, pp. 503–504.
27. *Op. cit.* 3, p. 504.
28. *Op. cit.* 22, p. 119.
29. Alkis Togias *et al.*, "Evaluating the Factors that Relate to Asthma Severity in Adolescents," *International Archives of Allergy and Clinical Immunology*, Vol. 113 (1997), pp. 87–95.
30. Curt Suplee, "Most Serious Youth Asthma Cases Linked to Roaches, Study Finds," *The Washington Post* (May 8, 1997), p. A12.
31. David L. Rosentreich *et al.*, "The Role of Cockroach Allergy and Exposure to Cockroach Allergen in Causing Morbidity Among Inner-City Children With Asthma," *The New England Journal of Medicine*, Vol. 336, No. 19 (1997), pp. 1358–1359.
32. *Op. cit.* 29, pp. 87–95.
33. Thomas A.E. Platts-Mills and Judith Woodfolk, "Rise in Asthma Cases," *Science*, Vol. 278 (November 1997), p. 1001.
34. Malcolm Sears and D. Robin Taylor, "The β2-agonist Controversy: Observations, Explanations, and Relationship to Asthma Epidemiology," *Drug Safety*, Vol. 11, No. 4 (1994), pp. 264–265.
35. *Op. cit.* 10.
36. *Op. cit.* 2, p. 130.
37. Ttaro Shirakawa *et al.*, "The Inverse Association between Tuberculin Responses and Atopic Disorder," *Science*, Vol. 275, No. 3 (1997), p. 77.
38. Erika von Mutius *et al.*, "Prevalence of Asthma and Atopy in Two Areas of West and East Germany," *American Journal of Respiratory and Critical Care Medicine*, Vol. 149 (1994), p. 363.
39. Peter Gergen and Kevin Weiss, "The Increasing Problem of Asthma in the United States," *American Review of Respiratory Disease*, Vol. 146 (1992), p. 824.
40. *Op. cit.* 2, p. 122.