Epidemiology of asthma: the year in review
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Asthma is a worldwide problem and there is evidence that the prevalence is increasing, but there are still insufficient data to determine the likely causes for this increase. Epidemiologic studies are the only way in which the risk factors associated with this disease can be measured in populations. Knowledge of prevalence and risk factors is important for resource allocation, for the design of interventions, and for the prevention of the development of disease at an early stage.

Asthma is defined as a clinical syndrome characterized by airway inflammation, variable lung function, and airways responsiveness [1]. Epidemiologic studies are hindered by having no clear definition of asthma, as there is no clinically accepted method for measuring inflammation, and it is unlikely that one will be possible until more is known about the pathogenesis of the condition. Despite these problems, in both clinical evaluation and epidemiologic research, asthma-like symptoms and the presence of atopy are heavily relied on to establish the diagnosis.

Prevalence
Whether any survey truly measures the prevalence of asthma is an important question. This is particularly true when discussing the question of whether asthma is becoming more common [2]. Most well-conducted studies suggest that the prevalence of asthma has been increasing in children and young adults for the last several decades by approximately 5% to 6% per year worldwide, but the prevalence among impoverished inner city children has been much higher [3••,4–7]. The prevalence of asthma has been tracked and described in many developed countries. The prevalence is generally estimated using questionnaires and physiologic studies. In the United States, the National Health Interview Survey and the National Health and Nutrition Examination Survey used random samples of the US population and were conducted by the National Center for Health Statistics, providing periodic prevalence estimates. The most recent estimates from late 1998 project state-specific prevalence rates of 5.8% to 7.2% [8] (Table 1). The Centers for Disease Control and Prevention Surveillance for Asthma report (1960–1995) used existing databases to evaluate self-reported asthma prevalence, asthma office visits, asthma emergency room visits, asthma hospitalizations, and asthma mortality. The findings show increases in self-reported asthma prevalence and asthma death rates in recent years, nationally and regionally [3••] (Table 2).
A study by Silver et al. [9] suggests that the prevalence of asthma among children actually may be underestimated based on diagnostic label alone. The study shows that children with wheeze alone and no diagnostic label of asthma were less often, but similarly affected by, repeat episodes, sleep disturbances, and attacks that limited speech. Another study, which characterized phenotypes in 92 two and three generation families with asthma, also showed that a large number of offspring with clinical evidence of asthma did not have a prior diagnosis of asthma by a physician [10].

Another important ongoing longitudinal cohort study is the International Study of Asthma and Allergies in Children (ISAAC), which is intended to establish a standardized method capable of facilitating international collaborative studies. It aims to describe the prevalence and severity of asthma, rhinitis, and eczema in school children in 155 centers in 56 countries [11]. Phase I has demonstrated a large variation in the prevalence of asthma symptoms in children throughout the world [12–14] (Fig. 1). More than 450,000 children aged 13 to 14 years were interviewed using one-page questionnaires or video asthma questionnaires. There were differences between 20- and 60-fold in the prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema with the highest prevalences from centers in the United Kingdom, Australia, New Zealand, and Republic of Ireland, followed by most centers in the Americas [12,13,15••,16,17]. Similar to other studies comparing reported symptoms and diagnosed asthma, there was a significantly lower frequency of diagnosed asthma compared with symptom reporting, suggesting that asthma is underdiagnosed [17].

Areas of low prevalence of asthma and atopic conditions have been identified in developing countries and in Eastern Europe. There has been much interest in the striking differences in the prevalence of atopic diseases between people living in Eastern and Western Europe. In 1995, 5 years after the German unification, a repeat prevalence study in Leipzig (former East Germany) was undertaken as part of the International Study of Asthma and Allergies in Children. In Eastern Germany, where drastic changes toward Westernization of living conditions have occurred after reunification, an increase in the prevalence of hay fever and atopic sensitization has been documented over the last 4 to 5 years in children between ages 9 and 10 years. The prevalence of asthma and airway hyperresponsiveness, however, remained virtually unchanged in this age group [12,18].

**Incidence**

Asthma incidence data are available from several cohort studies that describe incidence rates of 0.0% to 3.9% per year, consistently highest among the youngest age groups and among boys [19–24]. Toren and Hernmansson [25] recently reported asthma incidence in an adult Swedish population, defined as “physician-diagnosed” asthma by patient report. They found that the incidence rate for adult-onset asthma was highest among women, female smokers, and former smokers. As in prior studies, reported symptoms of atopy and family history of atopy were strongly associated with incidence of adult-onset asthma [25]. A large cohort of 11,540 Finnish participants, initially 18 to 45 years old, were followed from 1975 to 1990 as part of the Finnish Twin Cohort Study [26]. In this group, there was no significant increase in asthma incidence from 1982 to 1990 [26]. Hay fever and bronchitis usually were diagnosed before asthma. Both diseases increased the risk of asthma significantly on the basis of analyses of all individuals and of discordant twin pairs [26].

**Natural history**

The natural history of asthma has been descriptively characterized in the past. Important questions about
prognosis, the child who “may outgrow the disease,” rate of decrease in lung function, and risk factors can be addressed by these studies [27,28••,29,30]. There are several important ongoing cohort studies, one of which is the Childhood Asthma Management Program, which consists of 1041 children with mild to moderate asthma [28••]. A recent report analyzed data from this cohort to examine the relation between duration of asthma and severity of asthma. The data demonstrate that duration of asthma is associated with lower lung function, greater responsiveness to methacholine, more symptoms of asthma, and greater use of as-needed β-agonists, which are measures of asthma severity or control [28••].

Lessons from long-term cohort studies in the past have shown that most childhood asthma begins in infancy, with most children having their first episode of wheeze before age 3 years, and that viral infections may be critical in the development of asthma in childhood. One of the difficulties with the epidemiologic study of asthma is that there are various phenotypes with distinct characteristics, perhaps risk factors and prognoses [10,27,28••,29,30]. Future studies are needed to divide the broad spectrum of asthma into phenotypic groups to provide more precise information about cause and outcomes. One such study, which separates asthma, wheezy bronchitis, and atopy across two generations, found that children of wheezy bronchitic probands had a significantly better symptomatic outcome in adolescence, irrespective of the atopic status of the parent proband, than children of either asthmatic or asymptomatic probands, suggesting that this may be a syndrome that shows familial aggregation and is distinct from asthma [31]. These findings also suggest that some of the increase in asthma prevalence is associated with specific immunoglobulin E sensitization and is occurring in persons previously considered to be at low risk of developing asthma or atopy [31].

Asthma in adult and elderly asthmatic patients is less well studied, as epidemiologic research has focused largely on children and young adults. A recent review of the natural history of asthma in adults notes that asthma is progressive, leading to irreversible obstruction in 80% of elderly patients, and that deterioration in lung function develops faster in nonallergic patients with intrinsic asthma during the period shortly after onset of asthma and in older patients [32•]. Approximately 4% of patients in this cohort died of asthma and most were elderly [32•]. Another important longitudinal cohort study is the Normative Aging Study established by the Veterans Administration in 1961. The cohort consists of 2280 community-dwelling men from the greater Boston area who were 21 to 80 years old at the time of enrollment. The relation between home allergen exposure and decrease in forced expiratory volume in 1 second in 10 asthmatic and 30 randomly selected, age-matched, nonasthmatic participants were compared. In both groups, there was an accelerated decrease in forced expiratory volume in 1 second independent of airway
responsive and related to concentration of cockroach allergen [33]. In a Danish cohort, the Copenhagen City Heart Study, which included 17,506 adult participants of whom 1095 had self-reported asthma, the decrease in forced expiratory volume in 1 second among asthmatic patients was 38 mL/y, compared with 22 mL/y in those without asthma. Asthmatic patients also had greater decreases over time than those without asthma [34]. This supports prior evidence that asthmatic persons have greater decreases in lung function over time compared with nonasthmatic persons [35–37].

Environment
The prevalence of asthma in Westernized societies has increased steadily this century, doubling in the last 20 years. Although asthma is familial, however, with genome-wide searches having shown that many genetic loci predispose to the disease, it is unlikely that the genetic makeup of stable populations can change significantly in less than one century. The probable cause of the epidemic, therefore, must lie in the environment. In many regions of the world, asthma has increased just as the populations have become Westernized [13,18]. Air pollution may aggravate existing asthma, but it is unlikely responsible for the asthma epidemic. Comparisons have been made between the prevalence of asthma and allergy in highly polluted Leipzig in East Germany and clean Munich in West Germany [13,18,38,39]. Surprisingly, the prevalence of asthma and skin tests to common allergens was lower in the East until the German unification; now the former East Germany is experiencing increases in atopic disorders [13,18].

More recently, the association between long-term exposure to ambient air pollution and respiratory symptoms was investigated in a cross-sectional study in randomly selected population samples of adults at eight study sites in Switzerland (the Swiss Study on Air Pollution and Lung Diseases in Adults), and the effect of annual mean concentrations of air pollutants was analyzed [40]. Although the study found an association between long-term exposure to air pollutants and decrements in lung function in participants reporting respiratory symptoms and in symptom-free participants, with a similar magnitude of decrement in both groups, there were no associations with asthma or asthma symptoms [40].

Several recent studies have shown an association between air pollution and asthma exacerbations and hospital visits for asthma [41–45]. Although this finding does not address causality, it provides data to support that air pollution has an effect on acute asthmatic episodes.

There is a significant body of evidence linking tobacco smoke and respiratory symptoms during childhood [24,27,46–49]. Most recently, an extension of the Tucson Children’s Respiratory Study in Tucson, Arizona, assessed the effects of passive smoking on respiratory symptoms in a cohort of more than 1000 children born between 1980 and 1984 and who were followed from birth to age 11 years. Maternal prenatal, but not postnatal, smoking, was associated with current wheeze, independent of a family history of asthma, socioeconomic factors, and birth weight [50]. This transitory effect of maternal prenatal smoking on wheezing could be attributable to changes that affect the early stages of lung development [24,51].

Finally, although environment undoubtedly plays a major role in this disease, environmental modification is important in at least disease control if not also prevention. As part of a comprehensive environmental intervention, the National Cooperative Inner-City Asthma Study instituted an environmental intervention to reduce exposure to cockroach allergen in inner city homes. The intervention, however, failed to produce a decrease of cockroach allergen burden to clinically insignificant levels in a random subset of 48 homes undergoing cockroach extermination in the intervention group [52]. Although environmental modification is likely important in this disease, these results demonstrate that removal of cockroach allergen from the home environment will likely not be easy.

Morbidity and mortality
Not only is the prevalence of asthma increasing, there is also a startling increase in asthma mortality rates throughout the world. The United States and Canada have experienced a 25% increase in asthma mortality since 1960. Several hypotheses have been formulated to explain these increases. The first is that an increase in asthma severity increases the number of patients at risk for death. This could be related to nonuse or inadequate compliance with anti-inflammatory agents in younger patients. In addition, substandard evaluation of the severity of the asthma by patients and health care professionals also may contribute to this trend. A study by Jones et al. [53] showed that inaccessibility of acute care hospital services may increase the risk of asthma mortality, with a relative risk of 1.07 for each 10-minute travel time to receive acute care. In a study by Turner et al. [54], previously identified risk factors for fatal and near-fatal asthma in retrospective studies were confirmed. In this prospective case control study, risk factors for fatal and near-fatal asthma included being previously ventilated, being admitted to the intensive care unit, having a history of worse asthma during January and February, and having used air conditioning [54]. This study also confirms the findings of previous studies that there exists a dependence on the emergency department for initial care among patients requiring hospital care for asthma [54,55]. Few patients in this
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study visited a physician before admission to the hospital, indicative of missed opportunities to intervene earlier in their disease [54,55]. Among adult patients with asthma, women are more likely to be admitted and more likely to die from asthma. A study of the Multicenter Asthma Research Collaboration compared emergency department visits for acute asthma among women and men. Although men received less outpatient care and had worse pulmonary function, women were more likely to be admitted to the hospital and to report ongoing symptoms at follow-up [56].

Asthma prevalence, hospitalization, and mortality rates also vary by race, all being consistently higher in blacks than in whites, with between 10% and 23% of inner city US blacks having asthma compared with 4% to 5% of US whites [3•••]. The highest mortality rates for asthma are in inner cities, with target populations at highest risk being identified in the poorest neighborhoods, East Harlem in New York City and Cook County in Chicago [57–59]. A study conducted in Rochester, New York, evaluated socioeconomic variation and risk for asthma hospitalization. All 2028 asthma hospitalizations between 1991 and 1995 for children dwelling in Rochester, New York, were analyzed [60]. The study found that the marked socioeconomic and racial disparities in Rochester’s asthma hospitalization rates are largely attributable to higher incidence of severe acute asthma exacerbations, based principally on the worst oxygen saturation, among inner city children, rather than excess utilization by this group [60].

Summary

Epidemiologic data provide clues to the cause, patterns of occurrence, and risks for the development of asthma and related morbidity. Although numerous factors have been identified, it will take collaborative efforts that incorporate basic pathophysiologic, genetic, and epidemiologic research to better understand the increased prevalence and natural history of this disease.

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References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

• Of special interest

•• Of outstanding interest


This is the Centers for Disease Control and Prevention’s report on asthma prevalence from the National Health Interview Survey and the National Health and Nutrition Examination Survey. It contains excellent graphic presentations. http://ftp.cdc.gov/pub/Publications/mmwr/SS/SS4701.pdf


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29 This important study showed that duration of asthma is associated with lower lung function, greater responsiveness to methacholine, more symptoms of asthma, and greater use of rescue medications.


34 This article reviews the natural history of asthma in adults, noting that asthma is progressive and leads to irreversible obstruction in 80% of elderly patients.


37 A longitudinal epidemiologic study of the general population in a Danish city, the Copenhagen City Heart Study, analyzed changes over time in the forced expiratory volume in 1 second in adults with self-reported asthma and adults without asthma. People who identified themselves as having asthma had substantially greater decreases in the forced expiratory volume in 1 second over time than those who did not.


44 The Swiss Study on Air Pollution and Lung Diseases in Adults found no association between long-term air pollutant exposures and the natural history of asthma. There were decrements in lung function of the same magnitude in those with and without asthma.


51 An extension of the Tucson Children’s Respiratory Study assessed the effects of passive smoking. Maternal prenatal, but not postnatal, smoking was associated with current wheezing.


