A comparison of seasonal trends in asthma exacerbations among children from geographic regions with different climates

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ABSTRACT

Background: The fall peak in childhood asthma exacerbations is thought to be related to an increase in viral infections and allergen exposure when children return to school. Whether the seasonality of asthma attacks among children from different geographic regions follows similar trends is unclear.

Objective: To compare seasonal trends in asthma exacerbations among school-age children who lived in different geographic locations, with different climates, within the United States.

Methods: Hospital billing data bases were examined to determine the monthly number of school-age children who were hospitalized or treated in the emergency department (ED) for asthma exacerbations. Data from four cities within three states were compared. Climate data were obtained from archives of the National Climate Data Center, U.S. Department of Commerce.

Results: An annual peak in asthma exacerbations was observed during the fall months (September through November) among children who lived in Charlottesville, Virginia, as well as throughout the state of Virginia. An increase in exacerbations, which peaked in November, was observed for exacerbations among children who lived in Tucson, Arizona, and Yuma, Arizona. In contrast, exacerbations among children from New Orleans, Louisiana, increased in September but remained elevated throughout the school year. Although there was annual variation in the frequency of exacerbations over time, the seasonal patterns observed remained similar within the locations from year to year. A nadir in the frequency of attacks was observed during the summer months in all the locations.

Conclusion: Seasonal peaks for asthma exacerbations varied among the children who lived in geographic locations with different climates, and were not restricted to the beginning of the school year.

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Seasonal variations in the frequency of asthma exacerbations during childhood occur worldwide. Among preschool and older children, most of the seasonal information available has been derived from studies of children who lived in the United States, Canada, the United Kingdom, and northern Europe.^{1–7} These studies report an increase in wheezing attacks that are most pronounced during the fall months. Some studies also report an increase

in exacerbations in the spring.^{1,5} It is not clear, however, whether seasonal patterns for attacks of wheezing are the same among children who live in different geographic regions where climates and environmental conditions vary.

Several articles proposed that viral infections account for the increased frequency of asthma exacerbations in the fall when children return to school.^{3,4,8–11} Other studies indicate that exposure to environmental allergens, which vary in intensity at different times of the year, may also contribute to this peak.^{1,7} In this study, we postulated that seasonal patterns for hospital admissions as well as emergency department (ED) visits for asthma exacerbations would differ among school-age children who lived in locations with different climates and that these differences may have important therapeutic implications.

METHODS

Data Collection

The International Classification of Diseases, 9th Revision codes 493.00, 493.01, 493.02, 493.90, 493.91, and

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493.92 were used to determine the number of children who were admitted to the hospital or treated for asthma in an ED in each location. Our initial evaluation included school-age children, 6–10 years of age, who were treated in the ED at the University of Virginia Medical Center in Charlottesville, Virginia. Data were also collected by the Office of Planning and Market Research at the University of Virginia for 6- to 10-year-old children who were hospitalized for asthma at major medical centers throughout the state of Virginia. In addition, data were examined over the same time period in the ED at the University of Arizona Medical Center in Tucson, Arizona.

For the initial evaluation, we examined data bases that covered a period from January 1998 through December 2001 for children with asthma treated in the ED in Charlottesville and Tucson, and from January 1999 through December 2001 for asthma hospitalizations throughout the state of Virginia. Data that covered the same period were available for children ages 2 through 10 years who were hospitalized for wheezing at the Yuma Regional Medical Center in Yuma, Arizona. Information, available from September 2001 through August 2003, was also available for ED visits for asthma at the Medical Center of Louisiana, New Orleans (Charity Hospital) for children 6 through 10 years old. Climatologic data (*i.e.*, relative humidity, absolute humidity, annual precipitation, and temperature variations) that covered the same time period for these geographic regions were obtained from the archives of the National Climate Data Center, U.S. Department of Commerce. To further judge the annual reproducibility of seasonal peaks of asthma, the same International Classification of Diseases, 9th Revision codes were used to reexamine the pattern of exacerbations among children 6 through 10 years old who were seen in the ED in Charlottesville as well as hospitalizations for asthma throughout the state of Virginia (from July 2007 through December 2013) and in the ED in Tucson (from July 2007 through December 2010).

Statistical Methods

Data for the number of children who were admitted to the hospital or treated for asthma in the ED were analyzed by way of longitudinal negative binomial generalized estimating equation models, whereas the climate data were analyzed by way of longitudinal linear mixed-effects models. The software of the PROC GENMOD and the PROC MIXED procedures of SAS version 9.1.3 (SAS Institute Inc., Cary, NC) were used to conduct the generalized estimating equation and linear mixed-effects analyses, respectively.

RESULTS

Charlottesville and the State of Virginia

From January 1998 through December 2001, a fall peak in visits to the ED for asthma was observed at the University of Virginia in Charlottesville among children ages 6–10 years. During this period, there were 301 visits to the ED, 40% of which occurred during the fall (September–November) (Fig. 1 A). The mean number of monthly visits to the ED for asthma from September through November (in the fall) was significantly higher than the mean number of monthly visits from December through February (winter), March through May (spring), and June through August (summer), $p < 0.001$, $p = 0.016$, and $p < 0.001$, respectively (Supplemental Table 1). Similarly, a fall peak in hospital admissions for asthma and a smaller increase in the spring were observed annually throughout the state of Virginia between January 1999 and December 2001 (Fig. 1 B). In more recent years (between July 2007 and December 2013), the pattern of the spring and fall peaks has been similar for ED asthma visits at the University of Virginia and for asthma hospitalizations throughout the state (Fig. 1, C and D). Over this period, the pattern of spring and fall peaks has been consistent, whereas the magnitude of these seasonal peaks, which were similar for ED visits in Charlottesville and for hospitalizations in Virginia, has varied from year to year.

Tucson and Yuma, Arizona

In Arizona, the total number of visits by children with asthma to the ED at the Medical Center of the University of Arizona in Tucson was 517 from January 1998 through December 2001 (Fig. 2 A). The number of visits was lowest during the months of June and July, followed by a gradual increase in visits, which then peaked in November. The same pattern was observed for asthma hospitalizations at the Yuma Regional Medical Center in Yuma, Arizona, located in the far western part of the state (Fig. 2 B) (total hospitalizations = 939). More recent data obtained from the ED in Tucson at the University of Arizona Medical Center (July 2007 through December 2010) revealed a similar seasonal pattern around the month of November, which varied in magnitude annually, along with variable and more modest increases in ED visits earlier in the year, between February and April (Fig. 2 C).

New Orleans, Louisiana

Visits to the ED for asthma exacerbations among children (6–10 years of age) were recorded from September 2001 through August 2003 at the Medical Center of Louisiana in New Orleans (Charity Hospital; total visits = 1291). As noted in Charlottesville,

Figure 1. (A) The number of monthly visits to the University of Virginia Emergency Department (ED) among school children (6–10 years old) who lived in Charlottesville, Virginia (January 1998 through December 2001). (B) The number of monthly admissions to the hospital for asthma among children 6–10 years old in Virginia (January 1999 through December 2001). (C) The number of monthly visits to the University of Virginia ED among school children 6–10 years old who lived in Charlottesville, Virginia (July 2007 through December 2013). (D) The number of monthly admissions to the hospital for asthma among children 6–10 years old who lived in the state of Virginia (July 2007 through December 2013).

Tucson, and Yuma, a significant nadir in asthma visits to the ED at Charity Hospital was observed during the summer months, followed by an increase in asthma visits in September (Fig. 3). However there were no predictable peaks in monthly visits to the

ED during the remainder of the school year, and the mean of monthly visits to the ED during the fall was not significantly different from the mean of monthly visits recorded during the winter or spring. Because the ED at Charity Hospital in New Orleans is no

Figure 2. (A) The number of monthly emergency department (ED) visits for asthma among children 6–10 years old at the University of Arizona Medical Center, Tucson, Arizona (January 1998 through December 2001). (B) The number of monthly hospitalizations for asthma among children 2–10 years old at Yuma Regional Medical Center, Yuma, Arizona (January 1998 through December 2001). (C) The number of ED visits for asthma among children 6–10 years old at the University of Arizona Medical Center, Tucson, Arizona (July 2007 through December 2010).

longer treating children for asthma, more recent data (after Hurricane Katrina) were not available.

Climate Conditions

Climate conditions in Charlottesville, Tucson, Yuma, and New Orleans were evaluated from May 1998 through August 2003, which overlapped with the years during which the data for ED visits and hospitalizations were collected from these locations. Differences in the average monthly values for relative humidity, absolute humidity (dew point temperature), temperature, and precipitation measurements are shown in Supplemental Fig. 1, *a-d*. The average annual relative humidity was significantly higher in Charlottesville compared with Tucson ($p < 0.001$) and Yuma ($p < 0.001$), and also in New Orleans compared with Tucson ($p < 0.001$) and Yuma ($p < 0.001$) (Supplemental Fig. 1 *a*). Similarly, annual precipitation throughout the year was significantly higher in Charlottesville than in Tucson ($p < 0.009$) and Yuma ($p < 0.005$), and the same

Figure 3. The number of visits to the Medical Center of Louisiana, New Orleans (Charity Hospital) emergency department (ED) each month among school children ages 6–10 years old (September 2001 through August 2003).

was true in New Orleans compared with Tucson ($p < 0.008$) and Yuma ($p < 0.005$) (Supplemental Fig. 1 *b*). During the summer (June–August), when a nadir for asthma exacerbations occurred in all the locations, the absolute humidity and average monthly temperatures peaked in all four locations and were substantially higher compared with other seasons (Supplemental Fig. 1, *c* and *d*).

DISCUSSION

This study focused on school-age children who were treated in the ED or the hospital for asthma exacerbations in geographic locations known to have different climates. Previous publications reported fall and spring peaks when children are more susceptible to asthma exacerbations and need care in the hospital or ED.^{1,5,12} Consistent with these observations, an annual peak in asthma exacerbations was also observed during the fall in Charlottesville and in the state of Virginia from September through November as well as a smaller peak in the spring. In contrast, different seasonal patterns for asthma attacks were observed in Arizona and in New Orleans among children in the same age group. In Arizona (both in Tucson and Yuma), children with asthma experienced more frequent attacks later in the fall (most often peaking in November) approximately 2.5 months after school started, whereas no predictable variations in monthly visits to the ED were observed during the school year in New Orleans. The results demonstrated that seasonal patterns of exacerbations were not the same during the school year in the different geographic areas. Analysis of these data supported the recommendation that recognizing seasonal patterns locally within geographic regions may enhance efforts to treat children with asthma more effectively during periods when they are most likely to experience an attack.

An important objective of this study was to evaluate the consistency of seasonal patterns of asthma exacerbations in children that needed hospital care over time. In Charlottesville, as well as in the state of Virginia, the fall and a smaller spring peak in asthma exacerbations have been occurring among school-age children for years. This seasonal pattern was first noted in the pediatric ED at the University of Virginia in the early 1990s¹² and continues to recur in more recent years (July 2007 through December 2013). Notably, these fall and spring peaks have also been observed among 2- and 3-year-old children in contrast to the well-known midwinter peak of wheezing exacerbations induced by viral pathogens, such as respiratory syncytial virus, metapneumovirus, and influenza, seen annually in Virginia among children <2 years of age.^{12–14}

In a study from Ontario, Canada (a region with a colder and less humid climate), a sharp peak of asthma

exacerbations, defined as the “September epidemic” was observed annually when children returned to school.^{4,11} Although positive tests for rhinovirus have been detected frequently among children and young adults who experience exacerbations during the fall, this virus also plays a major role in provoking attacks of wheezing throughout the year.^{1,15} Thus, it is doubtful that rhinovirus infections alone caused the increase in asthma exacerbations during the fall when children returned to school.

In several studies of asthma exacerbations induced by rhinovirus, the risk for an attack increases substantially if patients with asthma are also allergic.^{1,2,16,17} These studies indicate that allergic inflammation, including high titers of allergen specific immunoglobulin E antibody, significantly increase the odds that rhinovirus will provoke an attack of asthma that requires hospital care.¹⁷ In keeping with this, exposure to dust-mite allergen indoors in Virginia increases substantially during the fall months when exposure to ragweed also increases in Virginia and the mid-Atlantic states.^{18,19} By comparison, *Alternaria* has been shown to be the strongest risk factor for allergic sensitization associated with asthma among children who lived in Tucson, Arizona.²⁰ A previous 20-year survey of exposure to *Alternaria* in Tucson revealed an annual seasonal peak in October and November, which overlaps with the peak in asthma exacerbations observed in Tucson and Yuma in this analysis.²¹ Taken together, allergen exposures that are likely to influence seasonal peaks differ in the regions studied. The implications are that a better understanding for seasonal allergen exposures at the local level by clinicians and patients may provide an opportunity to enhance preventive measures and seasonal compliance with asthma medications.

As judged by the data available from New Orleans (before Hurricane Katrina), ED visits for asthma did not show significant variations during the school year in this analysis. Analysis of these results indicated that compliance with asthma treatments during the school year in this geographic location would deserve emphasis. Although environmental exposures may have changed since then, persistent dust mite, cockroach, and mold growth, along with exposure to allergens produced by *Basidiomycete* species, has been reported in New Orleans, which has a climate characterized by persistent humidity.^{22,23}

Analysis of the data collected in this study confirmed significant differences in climate conditions among the locations studied. The effects of climate on the seasonal patterns of asthma exacerbations, as well as the direct and indirect effects of climate on exposures to aeroallergens and respiratory pathogens, are likely to be complex. Although beyond the scope of this analysis, several variables are likely to influence the effects of

climate on asthma exacerbations. These variables include (1) the influence of outdoor climate on the climate and allergen exposures indoors where children and adults spend most of their time; (2) seasonal changes in the duration of sunlight, which can affect pollination and mold growth; and (3) climate conditions, *e.g.*, potential evapotranspiration, which reflects the moisture content of soil, which can have profound effects on vegetation.

Notably, a nadir in asthma exacerbations that required hospital care during the summer months was observed in all the locations. This nadir coincided with annual peaks in absolute humidity and temperature, but environmental factors and the amount of time that children spend indoors versus outdoors during the summer needs further investigation. In future studies, more-frequent monitoring of climate and associated environmental factors in “real time” (*e.g.*, with personal monitors worn by individuals with asthma) may reveal associations that help predict symptom exacerbations. Moreover, air pollution and environmental tobacco smoke, are known to augment the severity and persistence of asthma symptoms.^{24–26} Although these factors may be less likely to vary seasonally in parallel with seasonal peaks of asthma exacerbations, climate factors and air pollution have been reported to have value in predicting asthma symptoms among elementary school children.²⁷

Challenges to consider in interpreting the results from this study included the selection of three regions in the United States with different climates. A more comprehensive study that includes other regions (*e.g.*, the Midwest and Northwest) would be of interest and also larger in scope. However, this study achieved the objective of demonstrating that regional differences exist, thus which favored the use of local regional information to enhance asthma care. Our interpretation of the results reflected the choice of The International Classification of Diseases, 9th Revision codes, which we used to monitor asthma exacerbations over time. The same codes were used in each location. Although the initial data collected from Charlottesville, Arizona, and New Orleans overlapped in time, the data from these locations did not start and stop at the same time points. However, the patterns of seasonal peaks observed in Charlottesville and Arizona changed only in intensity but otherwise remained the same when evaluated longitudinally.

This study also focused on more-severe exacerbations of asthma that led to hospitalizations or treatment in the ED, which account for a large proportion of health care dollars spent on asthma nationally. Whether the observed seasonal patterns, especially the intensity of peaks, varied to the same extent may among children with milder asthma exacerbations who were treated at home, in school, or in a physician’s

office was not addressed in this study. In addition, we did not study the teenage population or children who were home schooled or who attended schools with alternative attendance schedules (*i.e.*, that differed from the conventional school year that starts in the fall and ending in late spring). These pediatric populations warrant further study. In looking to the future, the effects of climate change on the prevalence and seasonal peaks of asthma exacerbations in the United States and worldwide will also be of significant interest.

CONCLUSION

Conventional thinking is that infection with rhinovirus is the main reason for the peak in asthma exacerbations when children return to school but does not explain why peaks also occur at other times of the year (*e.g.*, October and November in Arizona, and annually during the spring in Virginia). The observations from this study were in support of the premise that exposure to environmental aeroallergens at the time of a rhinovirus infection is likely to contribute significantly to seasonal peaks in asthma exacerbations, which vary geographically. Although the intensity of the peaks can vary from year to year, the pattern of seasonal asthma exacerbations within each geographic location was predictable as judged by the data collected over time in the states of Virginia and Arizona. In these locations, the risk for more serious asthma attacks caused by rhinovirus is likely to be greatest during months when allergen exposures increase.¹ In support of this hypothesis, the administration of omalizumab, an anti-immunoglobulin E monoclonal antibody used to decrease asthma attacks among those with moderate-to-severe disease, substantially reduced and nearly eliminated seasonal peaks of asthma exacerbations among inner-city children.^{7,28}

Taken together, these observations can have important clinical implications. First, decisions regarding asthma severity and control by using National Institutes of Health guidelines may be strongly influenced by the time of year when the patients are evaluated. Second, the use of local, geographic information to recognize seasonal changes in the frequency of asthma exacerbations, together with individual patient risk factors (*e.g.*, allergic sensitizations), should enhance efforts to optimize the treatment of children with asthma during periods when they are most likely to experience an attack. Third, more detailed studies of environmental exposures that change in parallel with seasonal epidemics of asthma can have the potential for improving our understanding of the etiology and prevention of exacerbations that require hospital care.

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