**History of Ear Infections and Prevalence of Asthma in a National Sample of Children Aged 2 to 11 Years**

*The Third National Health and Nutrition Examination Survey, 1988 to 1994*

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**Methods:** We analyzed data on 7,538 children aged 2 to 11 years who participated in the Third National Health and Nutrition Examination Survey to examine the cross-sectional associations of history of ear infections with prevalence of ever-diagnosed asthma and the prevalence of wheezing in the last year in US children.

**Results:** History of ear infections was significantly related to the lifetime prevalence of diagnosed asthma (prevalence odds ratio [POR], 1.57; 95% confidence interval [CI], 1.05 to 2.36) and to the prevalence of wheezing in the last year (POR, 1.70; 95% CI, 1.22 to 2.37) after controlling for potential confounding variables. The number of ear infections was linearly and significantly related to the risk of asthma and wheezing in the last year. Among children with no diagnosis of asthma, there was a significant association between a history of ear infections and any wheezing in the last year (adjusted POR, 1.55; 95% CI, 1.07 to 2.25).

**Conclusions:** Our study indicated strong and significant associations of a history of asthma and wheezing with the frequency of ear infections in a nationally representative sample of 7,538 children aged 2 to 11 years. These findings highlight the need for prospective studies to examine further the relationship between asthma and ear infections.

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**Key words:** asthma; children and adolescents; ear infections; epidemiology; prevalence; wheezing

**Abbreviations:** CI = confidence interval; NHANES = National Health and Nutrition Examination Survey; POR = prevalence odds ratio

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Asthma is one of the most common chronic conditions affecting children in the United States, with approximately 4.8 million children < 18 years of age having the disease. The prevalence of asthma in children has increased significantly from the mid-1970s to the mid-1990s. From 1980 to 1994, the prevalence of self-reported asthma increased by almost 160% in children aged 0 to 4 years, and by 74% in those aged 5 to 14 years. Although the exact causes of the rise in asthma rates are unknown, previous studies have found associations of a wide variety of factors with asthma, including family history of allergies, previous infections, environmental exposures, and psychological conditions.

Childhood infections have been increasingly linked to the development or exacerbation of asthma or atopic diseases, with several studies demonstrating an increased risk of asthma or respiratory symptoms in children who had repeated infections early in childhood. However, some studies have suggested an inverse relationship between early childhood infections and the risk of subsequent asthma and atopic diseases. Factors that have suggested that treating early childhood infections with several antibiotics may increase the risk of asthma or atopy in children.

Some studies have suggested that treating early childhood infections with several antibiotics may increase the risk of asthma or atopy in children. Ear infections are very common in early childhood, with approximately 69% of US children < 12 years of age reporting at least one ear infection in their lifetime.
Materials and Methods

Data

This study used data obtained from NHANES III, which was conducted from 1988 to 1994. A total of 33,994 persons aged ≥ 2 months participated in this national survey representing the civilian noninstitutionalized population of the United States. The survey used a stratified, multistage, cluster-sampling design. Participants or proxy respondents for children provided data on sociodemographics, health status, and family medical history during a household interview. Further details on the procedures of NHANES III have been published elsewhere.

Lifetime prevalence of asthma was determined in the NHANES III survey by the question “Did a doctor ever say that (child’s name) had asthma?” The survey asked whether the child has had wheezing or whistling in the chest at any time in the past 12 months. A positive response to this question was followed by a question about the number of episodes of wheezing or whistling the child has had in the past 12 months. History of ear infections was assessed by the question, “Did (the child) ever have an ear infection or earache?” A positive response was followed by the question, “How many times has (child’s name) had an ear infection or earache?” Responses to the latter question were coded in the survey as 1, 2, 3 to 5, and 6 or more.

For this analysis, as a proxy measure for socioeconomic status, we used the educational level of the family reference person (head of the household). Educational level was categorized as < 7 years, 7 to 12 years, or > 12 years. Race/ethnicity was defined as non-Hispanic white, non-Hispanic black, Mexican American, and other race (including other Hispanic, Asian, and Native American). Parental history of asthma or hay fever was determined by the question “Has either of the child’s biological parents ever been told by a doctor that he or she had asthma or hay fever at any age?”

Statistical Analysis

A statistical software package (SAS, version 8.0; SAS Institute; Cary, NC) was used for data management and to explore the characteristics of the sample. Another program (SUDAAN; Research Triangle Institute; Research Triangle Park, NC) was used to incorporate sampling weights and to account for the unequal probabilities of selection, oversampling, nonresponse, and the complex multistage cluster-sampling design. Using this latter program, weighted percentage distributions of asthma, wheezing in the past year, and history of ear infections were computed using the CROSSTAB procedure. χ² tests were performed to test the variations in the exposure and the outcome variables by levels of potential confounding variables. Univariate and multiple logistic regression analyses were conducted to examine the association of history of ear infections and the prevalence of lifetime asthma while adjusting for potential confounding factors.

We also used logistic regression models to examine the association of asthma and ear infections in children who had their first ear infection in the first year of life after excluding those who received a diagnosis of asthma in the first year of life. In this analysis, at least the first ear infection preceded the diagnosis of asthma, although it is possible that some ear infections (for children with more than one ear infection) occurred after the diagnosis of asthma.

The final multiple logistic regression models included gender, race/ethnicity, age, parental history of asthma or hay fever, maternal smoking during pregnancy, and level of education of the family reference person. We also explored the potential confounding effects of daycare attendance, poverty income ratio, birth weight, and body mass index. However, we did not include them in the final models because they did not alter the association between history of ear infections and lifetime prevalence of asthma. First, multiple logistic regression models were conducted using history of ear infections as a dichotomous variable (ie, ever vs never) to assess for confounding factors and to identify the best model describing the relationship between asthma or wheezing and ear infections in children. Then, history of ear infections was used as an ordinal variable of three levels (ie, none, one to two, and three or more ear infections) and five levels (ie, none, one, two, three to five, and six or more ear infections).

In addition, we used logistic regression analysis to describe the association of history of ear infections (independent variable) with the prevalence of wheezing (any vs none) in the year prior to the survey, the prevalence of recurrent wheezing (three or more episodes vs less than three episodes) in the year prior to the survey, and the prevalence of wheezing (any vs none) in the year prior to the survey in children without diagnosed asthma.

Results

The study population consisted of 7,538 children aged 2 to 11 years who had complete data on the variables included in this analysis. The mean age of the population was 6.0 years, and 49.80% were male children. Among participants, 27.82% were non-Hispanic whites, 31.97% were non-Hispanic blacks, and 35.33% were Mexican Americans. Approximately 18.23% of participants had a parental history of asthma or hay fever. The characteristics of the sample, the weighted lifetime prevalence of diagnosed asthma, the weighted prevalence of wheezing in the past year, and the weighted distribution of parent-reported history of ear infections are given in Table 1.

The prevalence of lifetime asthma diagnosis in the US children aged 2 to 11 years was 9.24% (Table 1). It was significantly higher for male children than for
female children (10.55% vs 7.87%, respectively). Non-Hispanic blacks reported a higher (but nonsignificant) prevalence of asthma (10.17%) than did non-Hispanic whites (8.88%) or Mexican Americans (8.77%). The prevalence of lifetime asthma varied significantly by age groups, with the lowest rate reported for children aged 2 to 3 years, and the highest rate reported for those aged 6 to 8 years. Additionally, participants with a parental history of asthma or hay fever reported a higher rate of asthma than did those without a parental history of asthma or hay fever (16.58% vs 6.85%, respectively; \( p < 0.0001 \)). Neither maternal smoking during pregnancy nor the educational level of the family reference person was associated with asthma in univariate and multivariate analyses, and neither confounded the relationship between asthma and ear infections in this particular study. However, these two variables were included in the final logistic regression model due to their known association with both the outcome as well as the exposure variables.

Approximately 72% of the US children aged 2 to 11 years reported a history of at least one ear infection in their lifetime (Table 1). The lifetime rate of ear infections was slightly higher (but was nonsignificant) for male children than for female children and was negatively (but nonsignificantly) related to age. Non-Hispanic whites reported the highest rate of ear infections (78.96%), followed by Mexican Americans (61.59%) and non-Hispanic blacks (59.46%). Furthermore, the education level of the family reference person was significantly and positively related to the rates of ear infections.

Table 2 provides prevalence odds ratios (PORs) and 95% confidence intervals (CIs) for the association of lifetime prevalence of asthma and history of ear infections.
In univariate logistic regression models, the rate of ear infections in children was significantly associated with an increased risk of asthma (POR, 1.63; 95% CI, 1.11 to 2.38) [Table 2]. This relationship remained significant even after adjusting for sex, age, race/ethnicity, parental history of asthma or hay fever, maternal smoking during pregnancy, and educational level of the family reference person (POR, 1.57; 95% CI, 1.05 to 2.36).

In both univariate and multivariate logistic regression models, there was a clear and significant dose-response relationship between the number of ear infections and the prevalence of asthma (Tables 1 and 2). The prevalence of asthma in children with three or more ear infections during their lifetime was approximately twice that reported for children with no prior history of ear infections (12.43% vs 6.58%, respectively [not shown]; unadjusted POR, 2.01; 95% CI, 1.32 to 3.09) [Table 2]. This relationship remained almost unchanged after adjusting for confounding variables (POR, 1.95; 95% CI, 1.22 to 3.11). When the history of ear infections was divided into five categories (none, one, two, three to five, and six or more ear infections), the dose-response relationship between asthma and the number of ear infections persisted ($p = 0.0016$ for trend), but the association was significant only for children who had six or more ear infections compared to those with no history of ear infections, after adjusting for confounding variables (POR, 2.31; 95% CI, 1.38 to 3.88) [Table 2].

When we limited the analysis to children who had their first ear infection in the first year of life and excluded those in whom asthma was diagnosed in the first year of life (4,887 children), history of ear infections was nonsignificantly associated with the prevalence of lifetime asthma (adjusted POR, 1.54; 95% CI, 0.71 to 3.38) [Table 3].

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**Table 2—Weighted Unadjusted and Adjusted Association of Lifetime Prevalence of Asthma With Parent-Reported History of Ear Infections in Children Aged 2 to 11 Years From the NHANES III 1988–1994**

<table>
<thead>
<tr>
<th>Ear Infections</th>
<th>Unadjusted POR</th>
<th>95% CI</th>
<th>p Value for Trend*</th>
<th>Adjusted POR†</th>
<th>95% CI</th>
<th>p Value for Trend*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>1.63</td>
<td>1.11–2.38</td>
<td>0.0013</td>
<td>1.57</td>
<td>1.05–2.36</td>
<td>0.0045</td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1–2</td>
<td>0.97</td>
<td>0.70–1.35</td>
<td>1.00</td>
<td>0.73–1.39</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>2.01</td>
<td>1.32–3.09</td>
<td>1.95</td>
<td>1.22–3.11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.88</td>
<td>0.57–1.34</td>
<td>0.95</td>
<td>0.62–1.44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>1.06</td>
<td>0.75–1.51</td>
<td>1.06</td>
<td>0.74–1.52</td>
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<td></td>
</tr>
<tr>
<td>3–5</td>
<td>1.55</td>
<td>0.94–2.57</td>
<td>1.56</td>
<td>0.92–2.63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 6</td>
<td>2.43</td>
<td>1.54–3.84</td>
<td>2.31</td>
<td>1.38–3.88</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on logistic regression analysis with the number of ear infections treated as an ordinal variable.
†Adjusted for sex, race/ethnicity, age, parental history of asthma or hay fever, maternal smoking during pregnancy, and educational level of family reference person.

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**Table 3—Weighted Unadjusted and Adjusted Association of Prevalence of Asthma With Parent-Reported History of Ear Infections in Children Aged 2–11 Years Who Had Their First Ear Infection in the First Year of Life After Excluding Those in Whom Asthma Was Diagnosed in the First Year of Life From the NHANES III Study 1988–1994**

<table>
<thead>
<tr>
<th>Ear Infections</th>
<th>Unadjusted POR</th>
<th>95% CI</th>
<th>p Value for Trend*</th>
<th>Adjusted POR†</th>
<th>95% CI</th>
<th>p Value for Trend*</th>
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<tr>
<td>Never</td>
<td>1.00</td>
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<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>1.45</td>
<td>0.77–2.73</td>
<td>0.1530</td>
<td>1.54</td>
<td>0.71–3.38</td>
<td>0.2056</td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
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<td></td>
</tr>
<tr>
<td>1–2</td>
<td>0.76</td>
<td>0.41–1.41</td>
<td>0.92</td>
<td>0.47–1.78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>1.62</td>
<td>0.83–3.16</td>
<td>1.70</td>
<td>0.74–3.93</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>0.75</td>
<td>0.29–1.95</td>
<td>0.98</td>
<td>0.36–2.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>0.76</td>
<td>0.39–1.50</td>
<td>0.87</td>
<td>0.43–1.75</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3–5</td>
<td>0.82</td>
<td>0.33–2.02</td>
<td>0.92</td>
<td>0.34–2.50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 6</td>
<td>2.19</td>
<td>1.09–4.40</td>
<td>2.24</td>
<td>0.95–5.25</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Based on logistic regression analysis with the number of ear infections treated as an ordinal variable.
†Adjusted for sex, race/ethnicity, age, parental history of asthma or hay fever, maternal smoking during pregnancy, and educational level of family reference person.
association was not significant, children with a history of six or more ear infections had an increased likelihood of doctor-diagnosed asthma compared to those with no history of ear infections (adjusted POR, 2.24; 95% CI, 0.95 to 5.25) [Table 3].

Approximately 19% of the US children aged 2 to 11 years had a history of wheezing in the past year. The prevalence of wheezing was significantly and negatively associated with age ( p < 0.0001) [Table 1]. The lifetime rate of ear infections was significantly associated with an increased risk of wheezing during the past year (unadjusted POR, 1.88; 95% CI, 1.38 to 2.56; adjusted POR, 1.70; 95% CI, 1.22 to 2.37) [Table 4]. Compared to children with no history of ear infections, the risk of wheezing in the past year was linearly and significantly associated ( p = 0.0026 for trend) with the frequency of ear infections after controlling for potential confounding variables. The adjusted PORs were 1.52, 1.65, 1.63, and 1.92, respectively, for one, two, three to five, and six or more ear infections (Table 4).

Similar findings were observed when the prevalence of recurrent wheezing (three or more vs less than three episodes) during the year prior to the survey was used as the dependent variable (unadjusted POR, 1.85; 95% CI, 1.36 to 2.51; adjusted POR, 1.66; 95% CI, 1.21 to 2.28) [data not shown]. There was also a significant dose-dependent association ( p < 0.0001 for trend) between the number of ear infections and the prevalence of recurrent wheezing. The adjusted PORs were 0.91, 1.19, 1.88, and 2.31, respectively, for one, two, three to five, and six or more ear infections (data not shown).

For children with no diagnosis of asthma (6,924 children), 14.09% had a history of wheezing in the year prior to the survey. The prevalence of wheezing without doctor-diagnosed asthma was highly and negatively related to age ( p < 0.0001). The prevalence rates were 23.02%, 15.10%, 13.45%, and 7.53%, respectively, for children aged 2 to 3 years, 4 to 5 years, 6 to 8 years, and 9 to 11 years (not shown).

In addition, there were significant associations of the lifetime history of ear infections with the prevalence of wheezing without doctor-diagnosed asthma (adjusted POR, 1.55; 95% CI, 1.07 to 2.25) and recurrent wheezing (adjusted POR, 1.32; 95%, 0.84 to 2.08) in the past year (data not shown).

### Discussion

This study showed a strong significant dose-dependent association between the frequency of ear infections and the lifetime prevalence of asthma. A history of recurrent ear infections (whether defined as three or more ear infections or six or more ear infections) significantly increased the likelihood of doctor-diagnosed asthma, even after controlling for several confounding variables. These results are in agreement with the findings of two previous studies\(^{24,37}\) based on data obtained from two national surveys that showed that a history of repeated ear infections was associated with increased rates of asthma in children. A previous study by Lieu and Feinstein,\(^{24}\) which also utilized data from NHANES III, included an incidental finding that asthma increased the risk of ear infections in children <12 years of age (unadjusted risk ratio for asthma, 1.17; 95% CI, 1.08 to 1.26). In that study,\(^{24}\) children with diagnosed asthma had a higher rate of recurrent ear infections (ie, three or more ear infections) [adjusted relative risk, 1.64; 95% CI, 1.32 to 2.09].

In another study on 5,818 children <6 years of age who participated in the 1988 National Health Interview Survey of Child Health, Hardy and Fowler\(^{37}\) examined the univariate relationship be-

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### Table 4—Weighted Unadjusted and Adjusted Association of Prevalence of Wheezing in the Past Year With Parent-Reported History of Ear Infections in Children Aged 2–11 Years From the NHANES III Study 1988–1994

<table>
<thead>
<tr>
<th>Ear Infections</th>
<th>Unadjusted POR</th>
<th>95% CI</th>
<th>p Value for Trend†</th>
<th>Adjusted POR†</th>
<th>95% CI</th>
<th>p Value for Trend†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>1.00</td>
<td></td>
<td></td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ever</td>
<td>1.88</td>
<td>1.38–2.56</td>
<td>0.0007</td>
<td>1.70</td>
<td>1.22–2.37</td>
<td>0.0073</td>
</tr>
<tr>
<td>1–2</td>
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<td>1.28–2.34</td>
<td>1.58</td>
<td>1.15–2.18</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>1.96</td>
<td>1.37–2.80</td>
<td>1.78</td>
<td>1.20–2.63</td>
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<tr>
<td>1</td>
<td>1.70</td>
<td>1.07–2.70</td>
<td>1.32</td>
<td>0.93–2.47</td>
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<tr>
<td>2</td>
<td>1.76</td>
<td>1.32–2.34</td>
<td>1.65</td>
<td>1.23–2.21</td>
<td></td>
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<tr>
<td>3–5</td>
<td>1.79</td>
<td>1.18–2.72</td>
<td>1.63</td>
<td>1.06–2.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 6</td>
<td>2.11</td>
<td>1.51–2.95</td>
<td>1.92</td>
<td>1.32–2.81</td>
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</tbody>
</table>

*Based on logistic regression analysis with the number of ear infections treated as an ordinal variable.
†Adjusted for sex, race/ethnicity, age, parental history of asthma or hay fever, maternal smoking during pregnancy, and educational level of family reference person.
tween repeated ear infections (as defined by respondents) during the year prior to the survey and history of asthma. The study indicated that repeated ear infections are more common in children with a history of asthma (odds ratio, 2.3; 95% CI, 2.1 to 2.6).

The findings of our study correspond, in part, with the findings of several previous studies reporting an increased risk of asthma in children who had repeated exposures to infectious agents in early childhood. A study by Bodner et al showed that the number of infections before the age of 3 years was significantly associated with the increased risk of asthma, after controlling for potential confounding factors. Another study of a random sample of 15,043 school children by von Mutius et al using the International Study of Asthma and Allergies in Childhood core questions indicated that repeated episodes of fever during the first year of life were related to the prevalence of asthma and the frequency of wheezing in the year prior to the survey. The strongest relationship was observed between having five or more episodes of fever and the prevalence of asthma and current wheezing. The prevalence of wheezing and chest tightness increased with an increasing number of different types of respiratory tract infections among children without asthma (p < 0.001).

In a prospective study by Sigurs et al, respiratory syncytial virus bronchiolitis during the first year of life increased the risk of asthma and sensitization to common allergens in the following 2 years, particularly in children with a family history of atopy or asthma. In another prospective study by Anderson et al, throat or ear infections or tonsillectomy increased the risk of asthma and wheezing illness after the age of 7 years. Respiratory infections also have been linked to the exacerbation of asthma symptoms. Our findings indicated a significant association between a history of ear infections and prevalence of wheezing (with at least one episode in the year prior to the survey) or prevalence of recurrent wheezing (three or more episodes of wheezing in the year prior to the survey) (data not shown). The dose-dependent association of recurrent wheezing in the past year with the number of ear infections was similar but was more significant than that observed for asthma as an outcome. The association of the prevalence of wheezing in the past year with the history of ear infections remained significant even when we limited the analysis to children without a prior diagnosis of asthma (data not shown). The observed association between wheezing and recurrent ear infections may be explained, at least partially, by the association between wheezing and respiratory tract infections, including otitis media or recurrent ear infections, which has been demonstrated in other studies.

Although persistent wheezers may have an increased likelihood of developing asthma later in life, the association between ear infections and wheezing does not necessarily indicate an association with asthma, and not all children who have asthma experience wheezing. Therefore, this study also may suggest that at least some of the association between asthma and ear infections may be due to the strong association between wheezing and ear infections.

It is also possible that specific pathogens that repeatedly invade the middle ear and cause recurrent ear infections may play a major role in the development of asthma or wheezing. Respiratory syncytial virus, which has been linked to the onset of asthma or wheezing, was the most common virus detected in the middle ear fluid in children with acute otitis media.

Another possibility is that antibiotics that are commonly used to treat ear infections increase the risk of asthma. This hypothesis was supported by the results of several other studies showing an association between antibiotic use in early childhood and the development of asthma or atopy later in life. Unfortunately, we do not know in our study whether all ear infections were treated by antibiotics. It also has been suggested that some reductions in childhood infections might be related to the current rise in the prevalence of allergic conditions (i.e., the hygiene hypothesis). The hygiene hypothesis is supported by studies suggesting inverse associations of early childhood infections with asthma and atopic conditions, and by studies showing that day care attendance, large household size, or having one or more siblings were linked to a reduced risk of asthma or atopy in children. Although several studies showed a protective effect of infections in early childhood on the risk of asthma or atopy, the evidence remains inconclusive and debated.

The current study demonstrated a positive relationship between the lifetime history of ear infections and the level of education of the family reference person, a finding that is consistent with the results of previous studies. This association might reflect the positive relationship between the educational level of the family reference person and day care attendance, which was linked to the likelihood of otitis media or recurrent ear infections by several studies, including our study. In addition, the children of well-educated parents also might have greater access to health care and more knowledge about the condition, and thus are more likely to report the condition.

Any interpretation of our findings should consider the potential sources of bias. First, because of the cross-sectional nature of the study, it is unclear...
whether asthma or asthma complications, which predisposed children to ear infections or frequent ear infections, altered the responsiveness of the immune system to cause asthma or asthma symptoms. Gamble et al.\textsuperscript{22} suggested that asthma might affect the entire mucociliary system in the respiratory tract, thus leading to otitis media in children. However, our finding that a history of six or more episodes of ear infection increased the likelihood of asthma, after controlling for confounding variables among children who had their first ear infection in the first year of life after excluding those who received a diagnosis of asthma in the first year of life, suggests that ear infections may precede the development of asthma. This is consistent with the findings of other studies\textsuperscript{6,9} indicating a positive relationship between repeated childhood fever and infection episodes, and the risk of asthma or atopy. Unfortunately, the current study is not prospective, and the temporal nature of the association between ear infections and asthma should be examined in prospective cohort studies.

Second, almost 95% of the children who had a history of ear infections were treated by a doctor or health professional (not shown). This repeated exposure to health professionals because of ear infections, as confirmed by other studies,\textsuperscript{53} might have introduced a diagnostic bias leading to a higher prevalence of asthma in children with repeated ear infections. In our study, the prevalence of asthma was higher in children who were treated for ear infections than in those with ear infections who were not treated for the condition (not shown). However, this difference may be attributed to the variation in the severity of ear infections and its subsequent role in the development of asthma.

Third, the data used for this analysis were collected retrospectively, and relied on parental recall of both the outcome (i.e., asthma status or wheezing in the past year) and the exposure (i.e., history of ear infections). In our study, the lifetime prevalence of ear infections decreased (nonsignificantly) by age. This may also be due to the rise in the prevalence rates of ear infections in US children\textsuperscript{29,32,46} and does not necessarily reflect a recall bias. Parents are more likely to recall health conditions that have had a major impact on their lives. Both asthma and frequent ear infections are major health problems in childhood affecting children and their families. The magnitude, consistency, and significantly strong dose-dependent associations of asthma and ear infections observed in our study, however, suggest that our findings may reflect real biological phenomena.

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