Antibiotic Prescribing During Pediatric Ambulatory Care Visits for Asthma

WHAT’S KNOWN ON THIS SUBJECT: There have been several recent trials evaluating the efficacy of antibiotics as an asthma therapy, but to date, national guidelines do not recommend them as an asthma therapy. Inappropriate antibiotic prescribing may lead to avoidable adverse events and bacterial resistance.

WHAT THIS STUDY ADDS: Antibiotics are prescribed during nearly 1 million US asthma visits annually when antibiotic need is undocumented. The frequent coprescription of systemic corticosteroids suggests that greater symptom severity increases this practice. Conversely, asthma education delivery is associated with decreased antibiotic prescribing.

OBJECTIVE: National guidelines do not recommend antibiotics as an asthma therapy. We sought to examine the frequency of inappropriate antibiotic prescribing during US ambulatory care pediatric asthma visits as well as the patient, provider, and systemic variables associated with such practice.

PATIENTS AND METHODS: Data from the National Ambulatory Medical Care Surveys and National Hospital Ambulatory Medical Care Survey were examined to assess office and emergency-department asthma visits made by children (aged <18 years) for frequencies of antibiotic prescription. *International Classification of Diseases, Ninth Revision* (ICD-9) codes were used to assess the presence of coexisting conditions warranting antibiotics. Multivariable logistic regression models assessed associations with the prescription of antibiotics.

RESULTS: From 1998 to 2007, an estimated 60.4 million visits occurred for asthma without another ICD-9 code justifying antibiotic prescription. Antibiotics were prescribed during 16% of these visits, most commonly macrolides (48.8%). In multivariable analysis, controlling for patient age, gender, race, insurance type, region, and controller medication use, systemic corticosteroid prescription (odds ratio [OR]: 2.69 [95% confidence interval (CI): 1.68–4.30]) and treatment during the winter (OR: 1.92 [95% CI: 1.05–3.52]) were associated with an increased likelihood of antibiotic prescription, whereas treatment in an emergency department was associated with decreased likelihood (OR: 0.48 [95% CI: 0.26–0.89]). A second multivariable analysis of only office-based visits demonstrated that asthma education during the visits was associated with reduced antibiotic prescriptions (OR: 0.46 [95% CI: 0.24–0.86]).

CONCLUSIONS: Antibiotics are prescribed during nearly 1 in 6 US pediatric ambulatory care visits for asthma, —1 million prescriptions annually, when antibiotic need is undocumented. Additional education and interventions are needed to prevent unnecessary antibiotic prescribing for asthma. Pediatrics 2011;127:1014–1021

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The National Asthma Education and Prevention Program guidelines specify that antibiotics should not be used as part of chronic asthma therapy or for acute exacerbations, with the exception of patients with comorbid bacterial infections such as pneumonia or sinusitis.1,2 Nonetheless, over the past several decades there has been great interest in and numerous studies evaluating the role of antibiotics as part of asthma therapy.3–5 Macrolide and ketolide antibiotics have been specifically evaluated because they are believed to have anti-inflammatory actions6–9 in addition to their antimicrobial activity, which includes effectiveness against Mycoplasma pneumoniae and Chlamydia pneumoniae, “atypical bacteria” that commonly infect the respiratory tract.10–13 The studies evaluating antibiotics as an asthma therapy have mixed results, showing inconsistent evidence of benefit, although common bacterial pathogens (eg, Streptococcus pneumoniae, Haemophilus influenzae, and Moraxella catarrhalis) are frequently present in the airways of wheezing children.14 In accordance, neither US3 nor international15 guidelines for asthma management currently recommend antibiotic treatment for asthma exacerbations.

We sought to determine how frequently clinicians in US ambulatory care settings are prescribing antibiotics during pediatric asthma visits in the absence of a documented comorbidity that would justify their use. Using a nationally representative database of ambulatory health care visits, we further sought to evaluate patient demographic, clinical, provider, and visit features that were associated with antibiotic prescribing. We hypothesized that children with greater illness severity would be more likely to receive inappropriate antibiotic prescriptions on the basis of chart documentation from their visits. We further hypothesized that younger children would be more likely to receive antibiotics because of greater diagnostic uncertainty and that nonpediatricians, who less frequently treat children, would be more likely to prescribe antibiotics. Identifying factors associated with unjustified antibiotic prescribing during pediatric asthma care could help guide future interventions designed to prevent unnecessary antibiotic use in these children.

METHODS

Data Source

Data from the National Ambulatory Medical Care Surveys (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) were examined to assess office and emergency department–based visits made by children (aged <18 years) for frequencies of antibiotic prescription during asthma visits from 1998 to 2007. The NAMCS is a nationally representative data set of visits to physician offices in the United States conducted by the National Center for Health Statistics.16 The NAMCS uses a 3-stage probability-sampling design. The first stage involves sampling within geographic regions, the second stage involves sampling physician practices within the regions, and the third stage involves sampling patient visits within each selected physician practice. Physicians who participate in the NAMCS during a specific year are not eligible to be selected again for participation for at least another 3 years. Visits are assigned a weight to enable extrapolation to determine national estimates for all aspects of the survey. For each patient visit, the data set includes demographic and clinical information, including medications prescribed and the reason(s) for the visit on the basis of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. Additional information includes physician specialty and participation of allied health professionals (eg, nurse practitioner, physician assistant, or registered nurse). Since 2001, the NHAMCS has included a data element asking physicians to indicate whether asthma education was provided during the visit.

The NHAMCS is another public-use database designed to collect data on the use and provision of ambulatory care services in hospital emergency and outpatient departments. The NHAMCS is a population-based stratified sample survey of emergency-department visits in US hospitals. The NHAMCS uses a 4-stage probability sampling to include geographic primary sampling units, hospitals within the primary sampling units, emergency departments within the hospitals, and patients within the emergency departments. National estimates are based on patient weighting assigned by the National Center for Health Statistics statisticians. The weight for each visit takes into account all sampling stages and is used to produce unbiased national annual estimates. Both the NAMCS and the NHAMCS are public-use data sets that are exempted from review by the University of California at San Francisco institutional review board.

Study Population

Ambulatory care visits by children (aged <18 years) with ICD-9 codes for asthma (493.x) as the first diagnosis were evaluated. ICD-9 codes also were used to determine whether a comorbidity or secondary diagnosis existed that would justify prescription of an antibiotic (Table 1). In brief, although the use of words such as “justified,” “unjustified,” or “inappropriate” to describe antibiotic prescription for individual cases may be debatable, the use of
such terms for analysis of this data set is consistent with other similar studies17–20 and with US and international guidelines for asthma care.2,15

Data Analysis

We determined the percentage of all pediatric, ambulatory, asthma-related visits during which an antibiotic was prescribed without being justified by a comorbid diagnosis for which antibiotics are typically indicated. Antibiotic class was categorized into macrolides, aminopenicillins, cephalosporins, and all other antibiotics. Bivariate analyses were conducted comparing visits with and without unjustified antibiotic prescription on the basis of patient, clinical, physician, and system factors. Patient demographic variables included gender, age, race, ethnicity, and insurance.

Age was collapsed into a 3-level categorical variable consistent with National Asthma Education and Prevention Program guidelines (age <5, 5–11, and ≥12 years) to capture differences in outcome by specific age groups. Race and ethnicity were combined to create 4 categories (white [non-Hispanic], black [non-Hispanic], Hispanic, and other). Insurance was examined in 2 groups (private and all other, eg, Medicaid, self-pay, no charge, or charity). Other patient-level predictors included measures of illness acuity, including prescription of oral corticosteroids or inhaled corticosteroids, performance of a chest radiograph, and presence of a fever (≥38.0°C). To assess seasonality, months of the year were grouped into 4 periods (June through August, September through November, December through February, and March through May). Whether asthma education was delivered also was included as a variable for visits in the NAMCS data set. The single physician-level characteristic included as a variable was specialty (pediatrics, emergency-department physician, or other). The single system-level variable was US Census region (Northeast, Midwest, South, or West).

We then performed multivariable logistic regression to identify independent predictors of unjustified antibiotic prescription. Independent variables that nominally were associated with antibiotic prescription ($\chi^2$ test, $P < .20$) were entered into the multivariable model. Estimates and 95% confidence intervals (CIs) were generated by accounting for the complex survey design. All variables included in the model had an adequate sample size of more than 30 visits to ensure stable estimates as per the National Center for Health Statistics recommendations, unless otherwise specified. An additional bivariate analysis compared visits with prescription of macrolide antibiotics (azithromycin, clarithromycin, and erythromycin) with visits where any other antibiotic was prescribed. The analyses were conducted using SAS 9.2 (SAS Institute, Cary, NC) and SUDAAN 10.0 (RTI International, Research Triangle Park, NC).

RESULTS

For the 10-year period between 1998 and 2007, there were 5198 ambulatory care visits for asthma among children younger than 18 years of age in the data set, representing an estimated 60.5 million visits across the United States. During 15.6% of these visits, an antibiotic was prescribed without a co-existing diagnosis to justify such a treatment course. This equates to an estimate of ~1 million pediatric ambulatory visits per year in the United States for asthma during which antibiotics may be inappropriately prescribed. When antibiotics were prescribed during these visits, macrolides were the class of antibiotics most commonly chosen (48.8%), followed by aminopenicillins (26.3%) and cephalosporins (20.6%). All other antibiotic classes combined to account for the remaining 6.3%.

Bivariate Analyses

Bivariate comparisons demonstrated that patient demographic variables (age category, race/ethnicity, gender, and insurance type) were not associated with unjustified antibiotic prescription at asthma visits (Table 2), but a seasonal trend existed for antibiotic prescribing ($P = .08$). Although antibiotics were prescribed during ~12% of visits in the spring and summer months, they often were more prescribed in the fall (September through November: 18.5% of visits) and winter (December through February: 20.3% of visits).

Several variables associated with asthma or illness severity were assessed for their relationship with antibiotic prescribing. Although the prescription of an asthma controller medication, presence of a fever, and obtaining a chest radiograph were not associated with unjustified antibiotic prescribing, the prescription of a systemic corticosteroid (in an oral, intramuscular, and intravenous form) was

<table>
<thead>
<tr>
<th>Infection Type</th>
<th>ICD-9-CM Codes Specific Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>680–686 and 035</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>595,0, 595.9, and 599.0</td>
</tr>
</tbody>
</table>

5–11, and diograph, and presence of a fever costs of steroids, performance of a chest radiograph, and presence of a fever.

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Antibiotics were prescribed during 26.3% of visits during which systemic corticosteroids were given compared with 13.1% of visits during which they were not prescribed.

Comparisons also were made for physician specialty and US region, with no significant differences in antibiotic prescribing between groups. Whether asthma education was provided at the visit was 1 final variable assessed only in the NAMCS data set for the years 2001–2007. It is noteworthy that although unjustified antibiotics were prescribed during 19.3% of visits when no asthma education was documented, they were prescribed during only 11.2% of visits during which asthma education was documented (P = .04).

### Multivariate Analyses

In multivariate analysis, controlling for patient age, gender, race, insurance type, US region, and controller medication use, systemic corticosteroid prescription (odds ratio [OR]: 2.69 [95% CI 1.68–4.30]), and treatment during the winter season (OR: 1.92 [95% CI: 1.05–3.52]) increased the likelihood of antibiotic use (Table 3), whereas treatment in an emergency department decreased the likelihood of antibiotic prescription (OR: 0.48 [95% CI: 0.26–0.89]). A second multivariate analysis of the NAMCS data set using only the years when asthma education was included as a variable (2001–2007) demonstrated that asthma education reduced the likelihood of unjustified antibiotic prescription (OR: 0.46 [95% CI: 0.24–0.86]). Systemic corticosteroid prescribing also was associated with an increased likelihood of antibiotic prescription in this model (OR: 2.13 [95% CI: 1.10–4.11]).

A subgroup multivariate analysis of visits for children younger than 5 years of age, controlling for the same variables as above, found similar results. Systemic corticosteroid prescription was associated with an increased likelihood of antibiotic use (OR: 2.46 [95% CI: 1.21–4.99]), whereas treatment by an emergency physician was associated with a reduced likelihood of antibiotic prescription (OR: 0.38 [95% CI: 0.15–0.96]).

### Associations With Antibiotic Choice

Within only those visits where antibiotics were prescribed, we sought to determine which variables were associated with the prescription of macrolide antibiotics compared with other classes. When systemic
corticosteroids and antibiotics were jointly prescribed, macrolides were the antibiotic class chosen in 68.9% of visits, whereas macrolides were only prescribed in 38.1% of encounters when systemic corticosteroids were not also administered (\(P = 0.004\)). A trend also was discovered between insurance type and antibiotic choice, with macrolides being prescribed in 54.9% of cases where an antibiotic was prescribed to a child with private insurance but only 37.6% of such cases for those without private insurance (\(P = 0.06\)). No other variable listed in Table 2 was associated with antibiotic choice.

### DISCUSSION

The results of this study demonstrate that unjustified antibiotic prescriptions are common during ambulatory care pediatric visits for asthma, occurring at nearly 1 in 6 such visits, with macrolide antibiotics accounting for roughly one-half of all antibiotics prescribed. The finding that overall antibiotic use, and specifically macrolide antibiotic use, occurs more commonly when systemic corticosteroids are jointly prescribed is in agreement with studies that have reported that disease severity has some influence on this choice.\(^{21,22}\) It is further possible that with increased disease severity, clinicians faced with diagnostic uncertainty (eg, acute asthma exacerbation versus bronchiolitis versus atypical pneumonia) may choose to treat multiple possible etiologies for the acute symptoms, although these data suggest that patient age does not increase the likelihood of such uncertainty as we had hypothesized.

Our findings raise similar concerns regarding antibiotic overuse and the associated impact on resistance as those using the NAMCS database to describe frequent antibiotic prescribing for colds, upper respiratory tract infections, and bronchitis in children.\(^{17–20}\) Also consistent with the data in this report, the use of broad-spectrum antibiotics and, specifically, macrolides for these conditions within NAMCS visits was common.\(^{20,23}\)

Others have used large data sets to evaluate antibiotic prescribing associated with asthma exacerbations. The study by Knapp et al,\(^{24}\) for example, used the NHAMCS to assess antibiotic prescribing at over 400,000 moderate to severe asthma exacerbations seen in the emergency department and found that 29% of such visits resulted in an antibiotic prescription. Although this figure is more than double the rate we found in emergency-department settings, that study did not evaluate whether comorbid diagnoses may have accounted for some antibiotic prescribing as other studies also have failed to do.\(^{25–29}\) Accounting for comorbidities was shown to be important by Vanderweil et al’s\(^{30}\) study of a sample of adults and children, which demonstrated that accounting for secondary diagnoses does reduce the proportion of visits with unjustified antibiotic prescriptions during emergency-department visits for asthma.

The lower frequency of antibiotic prescribing in the emergency-department setting was somewhat unexpected because nearly all emergency-department

### TABLE 3

<table>
<thead>
<tr>
<th>Multivariate Models of Factors Associated With Antibiotic Prescription at Ambulatory Care Asthma Visits</th>
<th>NAMCS and NHAMCS, 1998–2007, Adjusted OR (95% CI)</th>
<th>NAMCS, 2001–2007, Adjusted OR (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.99 (0.66–1.50)</td>
<td>0.99 (0.56–1.77)</td>
</tr>
<tr>
<td>Male</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>0.87 (0.53–1.33)</td>
<td>0.87 (0.43–1.76)</td>
</tr>
<tr>
<td>5–11</td>
<td>0.65 (0.39–1.06)</td>
<td>0.76 (0.38–1.51)</td>
</tr>
<tr>
<td>12–17</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Race/ethnicity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Non-Hispanic black</td>
<td>0.59 (0.35–1.02)</td>
<td>0.82 (0.30–2.28)</td>
</tr>
<tr>
<td>Hispanic</td>
<td>0.72 (0.41–1.26)</td>
<td>0.51 (0.23–1.14)</td>
</tr>
<tr>
<td>Other</td>
<td>0.71 (0.28–1.78)</td>
<td>1.06 (0.34–3.27)</td>
</tr>
<tr>
<td>Insurance type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Private</td>
<td>0.94 (0.65–1.36)</td>
<td>1.14 (0.64–2.04)</td>
</tr>
<tr>
<td>Nonprivate</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Region of United States</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Northeast</td>
<td>0.74 (0.38–1.46)</td>
<td>0.66 (0.23–1.88)</td>
</tr>
<tr>
<td>Midwest</td>
<td>1.10 (0.62–1.97)</td>
<td>1.18 (0.45–3.08)</td>
</tr>
<tr>
<td>South</td>
<td>1.49 (0.92–2.41)</td>
<td>1.81 (0.92–3.58)</td>
</tr>
<tr>
<td>West</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>Corticosteroid (orally/intramuscular/intravenous)</td>
<td>2.69 (1.88–4.30)</td>
<td>2.13 (1.10–4.11)</td>
</tr>
<tr>
<td>Controller medication</td>
<td>0.99 (0.65–1.50)</td>
<td>0.97 (0.52–1.81)</td>
</tr>
<tr>
<td>Season, month</td>
<td></td>
<td></td>
</tr>
<tr>
<td>June to August</td>
<td>Reference</td>
<td>Reference</td>
</tr>
<tr>
<td>September to November</td>
<td>1.56 (1.06–2.30)</td>
<td>1.66 (0.64–4.30)</td>
</tr>
<tr>
<td>December to February</td>
<td>1.92 (1.05–3.52)</td>
<td>1.73 (0.70–4.32)</td>
</tr>
<tr>
<td>March to May</td>
<td>1.04 (0.54–2.00)</td>
<td>1.47 (0.56–3.88)</td>
</tr>
<tr>
<td>Radiograph obtained</td>
<td>1.38 (0.77–2.45)</td>
<td>2.46 (0.33–11.35)</td>
</tr>
<tr>
<td>Physician specialty</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pediatrics</td>
<td>1.13 (0.66–1.93)</td>
<td>1.50 (0.71–3.14)</td>
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<td>Nonpediatrics and non–emergency department</td>
<td>Reference</td>
<td>Reference</td>
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<tr>
<td>Emergency-department physician</td>
<td>0.48 (0.26–0.89)</td>
<td>Reference</td>
</tr>
<tr>
<td>Time, year of visits</td>
<td>0.94 (1.07–1.01)</td>
<td>0.96 (0.83–1.11)</td>
</tr>
<tr>
<td>Asthma education</td>
<td>Reference</td>
<td>0.46 (0.24–0.86)</td>
</tr>
</tbody>
</table>

* Asthma education data were only available in NAMCS and only during these years.
visits for asthma are likely because of an exacerbation or increase in symptoms, whereas outpatient office visits may occur for reasons other than exacerbations, including follow-up of an exacerbation, medication management, lung function assessment, or symptom monitoring. Although the ability in emergency-department settings to rapidly obtain and review a chest radiograph theoretically could have explained the reduced frequency of antibiotic prescribing, the multivariate analyses did not support such an association nor did a previous patient study, which demonstrated that obtaining a radiograph was associated with more frequent antibiotic use. The differences between pediatrician and emergency-department physician prescribing may be related to clinical features not included in the NAMCS and NHAMCS databases, as described by Jenkins et al. Pediatricians from Northern Ireland in their study were more likely to use the presence of crepitations as a reason for antibiotic prescription but less likely to use the criteria of respiratory rate, air entry, and the child’s use of inhaled corticosteroids as reasons to prescribe antibiotics when treating a child with an asthma exacerbation compared with nonpediatricians. In addition, recent studies have shown that compared with visits to pediatricians, visits by children to emergency departments for respiratory tract infections are less likely to result in a prescription for a broad-spectrum antibiotic, suggesting possible differences in antibiotic prescribing practices between these specialties.

The National Asthma Education and Prevention Program guidelines recommend asthma patient education as a routine part of clinical care at every visit. Patient education should improve asthma self-management and knowledge of appropriate medications and their indications. We found that the delivery of asthma education was associated with reduced antibiotic prescribing for asthma visits in the NAMCS data set. This finding is consistent with others that have demonstrated a relationship between education and more judicious use of antibiotics for pediatric upper respiratory illnesses. Patient asthma education is increasingly being viewed as an important marker of quality of care in the ambulatory care setting. The results from this finding suggest other potential benefits for asthma education, as it seems to be associated with more judicious use of antibiotics by providers.

As with all studies describing large data sets, this study was limited to some extent by the data contained within it. It is probable that undocumented conditions that would have justified antibiotic prescribing existed to some extent within this sample. Other detailed information that may have guided the decision to prescribe antibiotics, such as presence of hypoxia, tachypnea, or inspiratory crackles was not available as variables for analysis. In addition, the lack of precision in the assignment of ICD-9 codes made it impossible to determine whether ambulatory visits for asthma were for exacerbations or other non-acute reasons related to asthma, although other studies similar to ours have used similar ICD-9 inclusion criteria to the present analysis.

Despite these limitations, the current study demonstrates that clinicians are prescribing antibiotics as part of asthma treatment in a fashion that conflicts with US and international guidelines. Potential explanations for this practice include diagnostic uncertainty, undocumented comorbid conditions, prophylaxis of secondary infections, an attempt to capitalize on the anti-inflammatory properties of macrolide antibiotics, and possibly the belief that colonization by, or infection with, noncultivable and/or unknown bacteria may be important in some patients with asthma. Until evidence supports the use of antibiotics for this purpose, however, clinicians may need guidance to improve and further research to inform their abilities to distinguish asthma exacerbations from those conditions that may benefit from antibiotics.

For those involved in practice management and physician education, this study documents a national rate of inappropriate antibiotic use for pediatric asthma that can be used to benchmark quality-improvement initiatives. Although this issue is challenging, several strategies to address provider antibiotic prescribing behavior have been shown to be effective in rigorous, randomized controlled trial designs. Physician education combined with a broader community-wide program was successful in improving antibiotic prescribing rates. Provider feedback and patient education also was successful in decreasing the rate of increase of inappropriate antibiotic prescribing. Although the interventions described did not focus specifically on antibiotic prescription during asthma visits, they suggest successful approaches that might be applied. In general, multifaceted interventions are more likely to be successful than single interventions focused on individual provider change.

CONCLUSIONS

Antibiotics are prescribed at nearly 1 in 6 pediatric ambulatory care visits for asthma when the need for antibiotics is undocumented, equating to ~1 million prescriptions annually in the United States. Because evidence does not currently support this practice, clinicians should consider national guidelines and eliminate unnecessary antibiotic prescribing for asthma exacerbations.
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