Antibiotic Prescribing for Canadian Preschool Children: Evidence of Overprescribing for Viral Respiratory Infections

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Antibiotic resistance is associated with prior receipt of antibiotics. An analysis of linked computerized databases for physician visits and antibiotic prescriptions was used to examine antibiotic prescribing for different respiratory infections in preschool children in Canada. In 1995, 64% of 61,165 children aged <5 years made 140,892 visits (mean, 3.6 visits per child) for respiratory infections; 74% of children who made visits received antibiotic prescriptions. Antibiotics were prescribed to 49% of children with upper respiratory tract infection, 18% with nasopharyngitis, 78% with pharyngitis or tonsillitis, 32% with serous otitis media, 80% with acute otitis media, 61% with sinusitis, 44% with acute laryngitis or tracheitis, and 24% with influenza. Acute otitis media accounted for 33% of all visits and 39% of all antibiotic prescriptions. The estimated Canadian-dollars cost of overprescribing was $423,693, or 49% of the total cost of antibiotics ($859,893) used in this group. This population-based study confirms antibiotic overprescribing in Canada.

In the 50 years since the introduction of penicillin, there has been the perception of control of many microbial diseases. However, in the 1990s, the rise of antimicrobial resistance among common organisms—such as the nonsusceptibility to penicillin of 25% of *Streptococcus pneumoniae* strains isolated in the United States [1] and of >50% of those isolated in Spain [2], Italy [3], and Hungary [4]—has caused alarm about the public health threat of emerging infectious diseases and antimicrobial resistance.

There is a strong association between prior receipt of antibiotics and development of antibiotic resistance [5–10]. Respiratory tract infections account for three-quarters of all antibiotic prescriptions [11]. Data collected from a pediatric group practice [12], a Kentucky Medicaid-claims database [13], and an analysis of pediatric antibiotic prescribing in the National Ambulatory Medical Care Survey [14] suggest that 50% of children who see a physician for a viral respiratory tract infection receive antibiotics.

The amount of increase in antibiotic prescription in Europe varies, with a lower rate in the United Kingdom than in Germany or France [15]. In Canada, the number of antibiotic prescriptions filled in 1996 was 26.3 million [16], in a total population of nearly 30 million [17]. To determine the magnitude of antibiotic prescribing for specific respiratory tract infections, data from the Saskatchewan Health Databases focusing on young children <5 years of age were obtained for the year 1995. This age group was targeted because children, particularly those <5 years of age, receive antibiotics more frequently than those in older age groups [18, 19]. We also examined patterns of use, costs of antibiotics, rates of inappropriate antibiotic prescribing, and associated hospitalizations.

**Methods**

**Saskatchewan Health Databases**

Saskatchewan, a province in western Canada, had a total population of 1,015,200 in 1995 [17]. As in all Canadian provinces, Saskatchewan residents have universal health care access through provincially funded health insurance. Physician claims, outpatient prescription-drug claims, hospital discharges, and health insurance registration can be linked across administrative databases and over time by means of the unique number assigned to each Saskatchewan Health beneficiary [20]. The administrative databases included prescribing information for the total population of Saskatchewan, with the single exception of registered American Indians. As of 30 June 1995, 61,165 registrants eligible for prescription drug benefits were <5 years of age.

Saskatchewan has a relatively restricted formulary for antibiotics for treatment of respiratory tract infections; it includes amoxicillin, ampicillin, penicillin V and G benzathine, cefaclor, cefuroxime, clarithromycin, and the
quinolones must fill in forms for “Exception Drug Status” coverage before their patients may receive these agents through the drug plan.

The above administrative databases were examined to extract a subgroup of patients whose diagnoses could be classified as respiratory tract infections with use of the International Classification of Diseases (ICD-9-CM) diagnostic codes [21]. Codes corresponded to the following diagnoses: serous (381) and acute suppurative (382) otitis media, common cold (460), acute sinusitis (461), acute pharyngitis (462), acute tonsillitis (463), acute laryngitis (464), acute upper respiratory tract infection (URI; 465), acute bronchitis or bronchiolitis (466), pneumonia (including viral, pneumococcal, and other bacterial pneumonia, pneumonia due to another specific organism, pneumonia without a causative organism specified, and bronchopneumonia) (480 – 486), and influenza (487).

Only one diagnostic code was allowed for each visit. If there were multiple diagnoses at the visit and an antibiotic was prescribed, it was assumed that the diagnostic code accurately reflected the infection most likely to be of bacterial origin and therefore likely to respond to antibiotics. An antibiotic prescription was attributed to a specific respiratory diagnosis when it was filled within 7 days of the physician-patient encounter. When there were several visits during a 7-day period, the prescription was attributed to the diagnosis made at the most recent visit. The cost of the prescription (which, for purposes of the study, consists of the acquisition cost, the markup, and the dispensing fee) was summarized in 1995 Canadian dollars.

**Appropriateness of Antibiotic Prescriptions**

Wherever possible, antibiotic appropriateness was determined on the basis of evidence-based guidelines. These included recent publications of a consensus group consisting of members of the Centers for Disease Control and Prevention (Atlanta), the American Academy of Pediatrics, and the American Academy of Family Practice, dealing with otitis media, nasopharyngitis, bronchitis, pharyngitis, and sinusitis [22–27]. In the guideline for pharyngitis, it was noted that 85% of acute pharyngitis is of viral etiology, for which antibiotics are not indicated [26].

For conditions not reviewed by the above group, further information was gathered from other consensus guidelines or reference textbooks. For many of the conditions, there have not been clinical trials of antibiotic management, which would offer evidence of the highest quality to indicate efficacy of an intervention [28]. In such situations, data on etiologic agents and appropriateness of antibiotics for treatment against such agents were used. However, these data constitute a lower level of evidence than that from randomized trials.

Acute bronchiolitis is a viral infection in which secondary bacterial infections are rare, and there is no benefit from antibiotic treatment, according to the single randomized clinical trial examining this question [29]. Thus, an expert Canadian consensus panel recommended against the use of antibiotics in initial management of bronchiolitis [30]. Another Canadian consensus panel has recommended against antibiotic treatment when viral pneumonia is suspected on the basis of epidemiological factors, presence of wheezing, or identification of viral etiology through antigen detection [31]. Otherwise, antibiotics are recommended.

A single ICD-9-CM code applies for acute laryngitis, croup, and tracheitis. Acute laryngitis is a viral infection, for which antibiotics are not indicated. Croup is managed with supportive therapy, racemic epinephrine, or systemic or inhaled steroids as necessary, but not antibiotics [32]. Both epiglottitis and bacterial tracheitis are bacterial infections for which antibiotics are indicated, but they are extremely rare and present as acute serious illness.

Therefore, we considered the following as inappropriate indications for antibiotics: nonspecific URI, the common cold, serous otitis media, acute bronchitis or bronchiolitis, laryngitis, and influenza; in addition, we considered 85% of antibiotics prescribed for pharyngitis or tonsillitis to be inappropriate. Given difficulties in differentiating etiologic agents in pneumonia, the heterogeneous nature of other respiratory infections, and the benefit of antibiotic treatment of acute otitis media and sinusitis, these conditions were considered appropriate indications for antibiotic treatment.

**Results**

A total of 140,892 visits were made during the 1995 calendar year by 38,848 children in Saskatchewan (3.62 visits per child), of whom 28,929 (74%) received at least one course of antibiotic. The number of visits and the frequency of antibiotic prescribing are listed in table 1. Because a subject may have had more than one physician visit for a diagnosis, the number of subjects and the frequency of prescribing per subject are also included.

Figure 1 shows the distribution of subjects prescribed antibiotics, according to illness syndrome and costs of those antibiotics. The most frequent reason for a visit and for an antibiotic prescription was treatment of acute otitis media, accounting for 39% of all antibiotics prescribed.

The penicillin class of antibiotics, including ampicillin, remains the most frequently prescribed. There was variation in the next most frequently used class of antibiotics, depending on the clinical diagnosis (figure 2). Specifically, trimethoprim-sulfamethoxazole (co-trimoxazole) was the next most frequently used agent for acute otitis media, and erythromycin was next most frequently used antibiotic for acute URI, pneumonia, and pharyngitis or tonsillitis.

The mean (±SD) antibiotic cost per patient, as shown in table 2, varied from $13.04 (±7.04) for a patient with a common cold to $23.84 (±21.08) for a patient with acute otitis media.
media. Patients with pneumonia were excluded from this comparison because the use of antibiotics in the hospital was not captured.

Associated hospitalizations for the same diagnosis within 30 days were generally uncommon. They occurred with 172 (0.4%) of the visits for acute URI; 53 (0.3%) of the visits for pharyngitis or tonsillitis; 371 (4.4%) of the visits for bronchitis or bronchiolitis; no visits for a common cold; 25 (0.5%) of the visits for serous otitis media; 223 (0.5%) of the visits for acute otitis media; 356 (9.4%) of the visits for acute laryngitis/tracheitis; 272 (6.4%) of the visits for pneumonia; 9 (0.4%) of the visits for influenza; no sinusitis visits; and 86 (2.2%) of the visits for other respiratory conditions. With the exception of acute bronchitis or bronchiolitis, acute laryngitis or tracheitis, and pneumonia, morbidity for the other syndromes is low, as indicated by low associated hospitalization rates.

If the evidence-based management guidelines were followed, antibiotics should have been withheld from all patients with acute URI, acute bronchitis and bronchiolitis, the common cold, influenza, serous otitis media, and acute laryngitis. One could also withhold antibiotics from 85% of those with acute tonsillitis or pharyngitis. Under these assumptions, 33,680 of a total of 66,419 courses of antibiotics (51%) could have been eliminated in 1995. The cost of overprescribing is in the order of $423,693, 49% of the $859,893 total expenditure for outpatient antibiotics for respiratory tract infections in this age group. Acute otitis media was the most common diagnosis contributing to antibiotic prescription costs, accounting for $369,296.

**Discussion**

Provincial health insurance allows Canadians to have return visits to their physicians without the burden of out-of-pocket costs.
costs, a practice that may lead to differences in the frequency of antibiotic prescribing as compared with that in the United States. The strength of these observations lies in the ability of the Saskatchewan Health Databases to capture the vast majority of all physician visits and outpatient antibiotic prescriptions. Our finding that 50% of antibiotics prescribed are not indicated on the basis of evidence-based guidelines is remarkably consistent with rates reported from the United States [11–13, 33].

In the United Kingdom, antibiotic prescribing increased by 46% between 1980 and 1991 [15], and overprescribing in general practice, especially for antibiotics, is estimated to cost 275 million pounds annually [34]. Half of all antibiotic prescriptions in the United Kingdom were for respiratory tract infections [35]. Thus, our findings likely have wide generalizability.

There were limitations to our study. The disease to which the antibiotic is attributed is dependent on the diagnostic code indicated on the physician claim form. For the purpose of determining antibiotic appropriateness, the listed diagnosis was assumed to be the indication for the antibiotic. Because claim forms allow only one disease code to be entered, it is possible that an uncoded illness was in fact the one for which antibiotics were indicated. We have observed in another study of prescribing by pediatricians for respiratory tract infection that these codes may be incorrect in up to 41% of cases when compared with chart diagnoses [36].

It was assumed that physicians’ diagnoses were correct. Physicians may diagnose certain conditions as bronchitis, sinusitis, or otitis media to justify antibiotic prescriptions [37, 38]. This would lead to an underestimate of inappropriate antimicrobial prescribing.

Another limitation of this study is the inability to capture antibiotic treatment initiated during a hospitalization. The low rates of antibiotic prescription for pneumonia, for example, are likely due to a selection bias to include milder cases or are due to capture of follow-up visits during recovery. One would predict that most patients with pneumonia had been hospitalized, and antibiotics initiated in that setting are not captured in the databases included in this study. It is assumed that many of the visits were follow-up visits, when no further antibiotic courses were being prescribed.

It is not possible to differentiate multiple visits for the same illness vs. single visits for illnesses recurring in the same year. Because physicians often have patients with acute otitis media or sinusitis return for follow-up visits, this may explain the low rate of prescribing for acute otitis media and sinusitis, as the second visit usually does not prompt a subsequent antibiotic prescription. Similarly, it is not possible to determine whether some of the antibiotic courses were prescribed only at the second visit, because of lack of improvement.

The estimate in the guidelines that 85% of pharyngitis cases are of viral etiology was based on studies that included older children [26]. In this population of young children, the proportion of pharyngitis that is viral in origin may be closer to 100%. Thus, the estimate of antibiotic overuse for viral infections may be low.

The relatively restricted formulary in Saskatchewan likely lowers the cost of agents and limits the variation in types of antibiotics prescribed through the drug plan. Where there is a larger number of drugs included in a formulary, one could predict greater use of newer, more expensive agents. Furthermore, actual prescribing may be underestimated in that the databases capture only antibiotic prescriptions that are actually filled; if prescriptions were not filled by families, they would not be noted in the database.

Only a single year was sampled, which fell during a period before media reports of increasing antibiotic resistance and of

### Table 2. Antibiotic treatment costs (in 1995 Canadian $), by diagnosis, for preschool children in Canada.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Mean cost/patient (SD)</th>
<th>Total antibiotic cost for 1995</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute URI</td>
<td>17.08 (11.97)</td>
<td>192,813</td>
</tr>
<tr>
<td>Acute bronchitis or bronchiolitis</td>
<td>16.37 (10.42)</td>
<td>58,017</td>
</tr>
<tr>
<td>Common cold</td>
<td>13.04 (7.04)</td>
<td>10,977</td>
</tr>
<tr>
<td>Serous otitis media</td>
<td>20.63 (15.51)</td>
<td>16,587</td>
</tr>
<tr>
<td>Acute laryngitis</td>
<td>14.25 (7.63)</td>
<td>16,744</td>
</tr>
<tr>
<td>Influenza</td>
<td>13.82 (6.75)</td>
<td>6,606</td>
</tr>
<tr>
<td>Acute pharyngitis or tonsillitis</td>
<td>16.83 (11.77)</td>
<td>143,475</td>
</tr>
<tr>
<td>Other respiratory condition</td>
<td>14.92 (9.11)</td>
<td>16,488</td>
</tr>
<tr>
<td>Acute otitis media</td>
<td>23.84 (21.08)</td>
<td>369,296</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18.46 (10.81)</td>
<td>23,133</td>
</tr>
<tr>
<td>Acute sinusitis</td>
<td>16.09 (13.19)</td>
<td>5,759</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>859,893</td>
</tr>
</tbody>
</table>

NOTE. URI = upper respiratory tract infection.
educational efforts aimed at reducing inappropriate antibiotic prescribing. A follow-up study is warranted to determine whether some of these educational and media efforts directed toward parents have substantially affected antibiotic prescription rates.

Comparisons of prescribing by type of physician (pediatrician vs. family practitioner) were not made. A higher rate of inappropriate antibiotic prescribing has been described with regard to family practitioners than to pediatricians in the management of acute laryngotracheobronchitis [39] and purulent nasopharyngitis [37]. However, in Saskatchewan, the majority of primary care of children is delivered by family practitioners, while pediatricians are mainly consultants.

Despite study limitations, the major contribution to antibiotic exposure is obvious for inappropriate antibiotic therapy for frequently seen nonbacterial conditions such as acute URI. With use of evidence-based guidelines, almost half of the costs incurred for antibiotic treatment of respiratory infections could have been saved. There was also inappropriate selection of antibiotics, which suggests a lack of differentiation between illness syndromes by some prescribers.

For example, ~6% of children with pharyngitis received trimethoprim-sulfamethoxazole, which would not be appropriate for treatment against group A streptococci. However, after penicillins there is a difference in the next most frequent antibiotic used for different syndromes, suggesting that most physicians do consider the syndromes different. Such substantial savings would be supplemented by the savings associated with the occurrence of fewer infections due to antibiotic-resistant organisms, which cause twice as much morbidity and mortality than susceptible organisms causing the same infections [40].

A number of factors other than the clinical condition influence antibiotic prescribing. Such factors include lack of certainty of diagnosis [41], heavy workload and inadequate time for each patient [42], fear of litigation for not treating a bacterial infection, the belief that antibiotics are innocuous, social and psychological characteristics of the patient [43], and perceived pressure from parents to prescribe [44–46]. Guidelines must be adapted for use in the office-based setting, with recognition of the existence of these potential obstacles. The acceptance of these practice guidelines by both the general public and physicians may be enhanced if the guidelines stress the harm of inappropriate antibiotic prescription [22].

Acknowledgments

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References

46. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? J Fam Pract 1996;43:56–62.