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# Principles of Judicious Use of Antimicrobial Agents for Pediatric Upper Respiratory Tract Infections

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**ABSTRACT.** This article introduces a set of principles to define judicious antimicrobial use for five conditions that account for the majority of outpatient antimicrobial use in the United States. Data from the National Center for Health Statistics indicate that in recent years, approximately three fourths of all outpatient antibiotics have been prescribed for otitis media, sinusitis, bronchitis, pharyngitis, or nonspecific upper respiratory tract infection.<sup>1</sup> Antimicrobial drug use rates are highest for children<sup>1</sup>; therefore, the pediatric age group represents the focus for the present guidelines. The evidence-based principles presented here are focused on situations in which antimicrobial therapy could be curtailed without compromising patient care. They are not formulated as comprehensive management strategies. For most upper respiratory infections that require antimicrobial treatment, there are several appropriate oral agents from which to choose. Although the general principles of selecting narrow-spectrum agents with the fewest side effects and lowest cost are important, the principles that follow include few specific antibiotic selection recommendations. *Pediatrics* 1998;101:163–165; antimicrobial resistance, antimicrobial use, upper respiratory infection, otitis media, pediatrics, sinusitis.

## THE IMPORTANCE OF JUDICIOUS ANTIMICROBIAL USE AND NEED FOR SPECIFIC PRINCIPLES

The emergence of bacterial strains that are increasingly resistant to antimicrobial agents is a growing national and worldwide concern. The specter of a "post-antimicrobial era," raised several years ago,<sup>2</sup> has been given credence by the spread of organisms such as vancomycin-resistant enterococci and multidrug-resistant tuberculosis, both essentially untreatable with routinely available antibiotics. Such infections remain primarily confined for the present to populations with special vulnerability, such as those in hospital intensive care units or high-risk populations in the inner cities. Practitioners may more frequently encounter treatment dilemmas resulting from organisms such as multiply drug-

resistant *Neisseria gonorrhoea*, *Shigella dysenteriae*, or *Pseudomonas aeruginosa*.

Antimicrobial resistance among respiratory pathogens has become a common clinical problem and its management a part of routine office practice. Currently, ~90% of *Moraxella catarrhalis* and 25% of nontypeable *Haemophilus influenzae* produce  $\beta$ -lactamase,<sup>3</sup> requiring treatment with  $\beta$ -lactamase-stable cephalosporins or combination drugs that include  $\beta$ -lactamase inhibitors such as amoxicillin-clavulanate.

The sense of urgency for the control of resistance in community-acquired pathogens has come in response to the recent dramatic emergence of illness caused by multiply drug-resistant *Streptococcus pneumoniae*. In the United States, the pneumococcus was almost universally sensitive to penicillin until the 1980s. In the last several years, however, there has been a rapid increase in the number of strains resistant to penicillin, extended-spectrum cephalosporins, and many other antibiotics. In 1994 in Atlanta, ~25% of invasive pneumococcal isolates were nonsusceptible to penicillin, and 9% were resistant to cefotaxime.<sup>4</sup> In response to this growing problem, control of the spread of antimicrobial resistance has been identified as a priority by many organizations, including the Centers for Disease Control and Prevention, the American Society for Microbiology, the World Health Organization, the American Academy of Family Physicians, and the American Academy of Pediatrics.<sup>5-7</sup>

The widespread use of antimicrobials, whether appropriate or inappropriate, has driven the emergence and spread of resistant organisms. The association of resistance with the use of antibiotics has been documented in both inpatient<sup>8</sup> and outpatient<sup>9</sup> settings. For example, more than five cross-sectional studies have documented that the likelihood of culturing a resistant strain of pneumococcus from the nasopharynx is increased if the patient recently completed a course of antibiotics.<sup>9-14</sup> More importantly, among patients with invasive pneumococcal disease, recent antibiotic use has been identified as a risk factor for infection with multiply drug-resistant strains in more than seven studies that have addressed this question.<sup>10,15-21</sup> This process can be reversed through judicious use of antibiotics, as illustrated by the observation that terminating  $\beta$ -lactam antibiotic prophylaxis and thereby reducing selective pressure leads to a reduction in the proportion of patients

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with  $\beta$ -lactam antibiotic resistant nasopharyngeal flora.<sup>22</sup>

Children can be protected from resistant bacteria through the judicious use of antimicrobial agents by their health care providers. This is the message that will be most persuasive in discussions between patients and care givers: not that withholding antibiotics should be advocated for the benefit of the community as a whole, but that unnecessary antibiotic use increases the individual patient's risk that infection will be caused by drug-resistant organisms.

#### WHY PRINCIPLES FOR JUDICIOUS ANTIMICROBIAL USE NOW?

Practice guidelines have proliferated in recent years, and US practitioners have been inundated with more than 1800 sets of guidelines.<sup>23</sup> It is important that the present set of principles are evidence-based and that they have been developed in an effort to improve both patient care and the public health, as opposed to containing costs or restricting care. They were developed in response to concern from professional organizations, physicians, and public health officials about the need to promote "judicious antibiotic use."<sup>5,6,24</sup> The principles that follow represent a multispecialty collaborative effort among members of Centers for Disease Control and Prevention, American Academy of Pediatrics, and American Academy of Family Physicians to assist local groups that are developing their own guidelines for appropriate use of antibiotics.

Efforts have been made to ensure that the following principles are based on scientific evidence from peer-reviewed literature. For each of the five conditions, searches of Medline were conducted for English-language articles published from January 1966 through July 1996. Search words were related to the disease entity and the specific question of interest (for example, "otitis media/prevention and control" and "prophylaxis") and the results supplemented by reviewing articles from bibliographies of textbooks, review articles, and symposium publications. Abstracts and unpublished work were excluded. Emphasis was placed on randomized controlled trials of antimicrobial therapy, studies that included a placebo group, studies with strictly defined diagnostic criteria or bacteriologic confirmation, and studies among pediatric patients. In some instances, trials among adults, studies with small sample sizes, or descriptive studies were considered; these instances are noted.

The development of principles alone is unlikely to evoke substantial change. Widespread adoption into routine clinical practice will occur only through concerted and sustained efforts to disseminate and promote these messages at national and local medical meetings. In addition, endorsement by the major professional organizations as well as by regional and local opinion leaders will be necessary. However, changes in practice are most likely to result if input from local practitioners is considered.<sup>25,26</sup> Therefore, we anticipate that these principles will serve as a basis for the local development and promotion of practice guidelines. Improving antimicrobial use also

will require effective communication with patients and parents about when antibiotic therapy is or is not needed. Most importantly, practitioners must see these principles as sensible and believe the goal of controlling antimicrobial resistance worthy of the efforts required to curtail antibiotic use.

Currently, millions of courses of unnecessary antibiotics are given each year. From 1990 to 1992, almost one in six physician office visits resulted in an antimicrobial prescription. These included >17 million prescriptions for nonspecific upper respiratory infection, 16 million prescriptions for bronchitis, and 13 million prescriptions for pharyngitis.<sup>1</sup> In a recent review of the Medicaid database in Kentucky, 60% of patients diagnosed with the common cold were treated with an antibiotic.<sup>27</sup>

Physicians report many pressures to prescribe unnecessary antibiotics, but most often cited is the unrealistic expectation for antibiotics on the part of patients or parents.<sup>28</sup> However, most parents do not acknowledge that they pressure their physician for antibiotics.<sup>28</sup> An important recent finding was that patient satisfaction with an office visit for respiratory infections was correlated with the quality of the patient-physician interaction but not with the prescription of an antibiotic.<sup>29</sup> A national campaign to improve parental and patient awareness about antimicrobial resistance and unnecessary antibiotic use is underway.<sup>30</sup> Improved understanding by the general public as well as the realization by physicians that patient satisfaction is not dependent on prescribing an antibiotic should help conscientious physicians in their efforts to restrict antibiotic overuse.

If unnecessary antibiotic use can be curtailed, there are indications that the community as well as the individual patient will benefit. In Japan, a remarkable 62% of group A streptococcal isolates were resistant to erythromycin in 1974, when macrolides accounted for 22% of all antibiotic use. By 1988, macrolides accounted for only 8% of antibiotic use, and <2% of group A streptococcal isolates were resistant to erythromycin.<sup>31</sup>

Similar observations have now been reported for resistant pneumococci as well. Reviews of antibiotic resistance patterns in Spain and Iceland have shown a correlation between those regions with the lowest antibiotic use and those with the lowest rates of penicillin-resistant pneumococci.<sup>32,33</sup> A small study of colonization with pneumococci among day care center attendees in Omaha, although uncontrolled for the effects of season and other factors, demonstrated a striking decrease in the proportion of children with resistant strains—from 53% to 7%—concomitant with a decrease in antibiotic use by the attendees.<sup>34</sup> In Iceland, publicity campaigns directed at the problem of pneumococcal resistance and its relationship to antibiotic use resulted in a decrease in sales of antimicrobial agents and a concomitant decrease in the prevalence of resistant pneumococcal isolates.<sup>35</sup>

Reducing the spread of resistant bacterial pathogens through judicious antimicrobial use is good for the individual patient and community and is feasible. The specific principles outlined in the accompa-

nying documents are a first step toward accomplishing this objective.

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## Otitis Media—Principles of Judicious Use of Antimicrobial Agents

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**ABSTRACT.** Otitis media is the leading indication for outpatient antimicrobial use in the United States. Overdiagnosis of and unnecessary prescribing for this condition has contributed to the spread of antimicrobial resistance. A critical step in reducing unnecessary prescribing is to identify the subset of patients who are unlikely to benefit from antibiotics. Conscientiously distinguishing acute otitis media (AOM) from otitis media with effusion (OME), and deferring antibiotics for OME will accom-

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