

## Principles of Appropriate Antibiotic Use for Treatment of Nonspecific Upper Respiratory Tract Infections in Adults: Background

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The following principles of appropriate antibiotic use for adults with nonspecific upper respiratory tract infections apply to immunocompetent adults without complicating comorbid conditions, such as chronic lung or heart disease.

1. *The diagnosis of nonspecific upper respiratory tract infection or acute rhinopharyngitis should be used to denote an acute infection that is typically viral in origin and in which sinus, pharyngeal, and lower airway symptoms, although frequently present, are not prominent.*

2. *Antibiotic treatment of adults with nonspecific upper respiratory tract infection does not enhance illness resolution and is*

*not recommended.* Studies specifically testing the impact of antibiotic treatment on complications of nonspecific upper respiratory tract infections have not been performed in adults. Life-threatening complications of upper respiratory tract infection are rare.

3. *Purulent secretions from the nares or throat (commonly observed in patients with uncomplicated upper respiratory tract infection) predict neither bacterial infection nor benefit from antibiotic treatment.*

*Ann Intern Med.* 2001;134:490-494.

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Upper respiratory tract infections (including the common cold) represent an important target for improving appropriate antibiotic use in ambulatory practice. In 1995, upper respiratory tract infection was the most frequent reason for seeking ambulatory care in the United States, resulting in more than 37 million visits to physician practices and emergency departments (1). Antibiotics are frequently prescribed for upper respiratory tract infections. The National Ambulatory Medical Care Survey, which specifically instructs participating physicians and staff on accurate diagnosis-coding procedures, revealed rates of antibiotic prescription for uncomplicated upper respiratory tract infection of 52% (2). Upper respiratory tract infection is the second leading condition for which antibiotics are prescribed each year, and it accounts for 10% of all antibiotics prescribed annually in ambulatory practice (3).

The overuse of antibiotics for upper respiratory tract infections has prompted attempts to better understand this practice. Physicians have reported that unrealistic patient expectations, patient pressure to prescribe antibiotics, and insufficient time to educate patients about

the ineffectiveness of antibiotics are some of the reasons why antibiotics are prescribed for upper respiratory tract infections (4). However, the clinical presentation of patients also appears to affect the decision to prescribe antibiotics for upper respiratory tract infection. A study that used a standardized symptom and physical examination recording form concluded that clinicians identify and treat with antibiotics a subset of upper respiratory tract infections primarily characterized by the presence of purulent manifestations (5). Purulent or green nasal discharge (reported or observed), production of green phlegm, presence of tonsillar exudate, and current tobacco use were independent predictors of antibiotic treatment of upper respiratory tract infection. In this study, 82% of patients prescribed antibiotics had at least one of these factors, and a significant linear relationship was observed between the number of factors present and the likelihood of antibiotic prescription. These findings are consistent with those of a physician survey in which respondents were more likely to prescribe antibiotics for hypothetical cases of upper respiratory tract infection when purulent nasal discharge was present (6).

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In addition to the Centers for Disease Control and Prevention, the principles outlined in this document have been endorsed by the American Academy of Family Physicians, the American College of Physicians–American Society of Internal Medicine, and the Infectious Diseases Society of America.

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The goals of this paper are to provide evidence-based recommendations for when to apply the diagnosis of upper respiratory tract infection and when to consider antibiotic treatment of adults with an uncomplicated upper respiratory tract infection. The background to, rationale for, and methods used to develop these principles are published separately (7).

## 1.0 RECOMMENDATIONS

*Recommendation 1. The diagnosis of upper respiratory tract infection should be used to denote an acute infection that is typically viral in origin and in which sinus, pharyngeal, and lower airway symptoms, although frequently present, are not prominent [B].* (Letters in square brackets are evidence ratings. See the background document in this issue [7] for explanation.)

1.1 Classification of patients with acute respiratory tract infections has traditionally been based on the anatomic localization of the prominent clinical signs and symptoms accompanying the illness (for example, sinusitis, pharyngitis, bronchitis, otitis media, and nasopharyngitis [the common cold]), and the diagnosis of “upper respiratory tract infection” has been reserved for cases with no prominent localizing features (8). It is very likely that clinicians vary in how they apply this taxonomy, since professional society recommendations for diagnosis of upper respiratory tract infection also vary. The International Classification of Health Problems in Primary Care defines “upper respiratory tract infection” as acute inflammation of nasal or pharyngeal mucosa in the absence of other specifically defined respiratory infection. Alternatively, the American Thoracic Society (9) and the Medical Research Council (United Kingdom) (10) recommend classification systems that do not include upper respiratory tract infection as an option. For example, the Medical Research Council provides the following options for classifying acute respiratory illnesses: common cold, otitis media, pharyngitis (including tonsillitis), laryngitis, croup, tracheitis, bronchitis, bronchiolitis, pneumonia, and influenza.

1.2 Evans (8) has conducted numerous studies of the microbiology of acute respiratory syndromes. He defines upper respiratory tract infection as “an undifferentiated clinical picture whose classification is based largely on the *absence* [italics added] of predominating features: thus the nose doesn’t run enough, the throat is not sore

nor red enough, and the cough is not severe nor paroxysmal enough to classify the illness as one of the other respiratory syndromes.” With rare exceptions, upper respiratory tract infections have a viral cause (11–13). When symptoms are severe, and particularly when they are accompanied by muscle ache and fatigue, influenza and parainfluenza infections are the most common causes, whereas rhinoviruses predominate when symptoms are mild. Other agents that are important causes of upper respiratory tract infection syndromes in adults include adenovirus and respiratory syncytial virus.

1.3 Most cases of uncomplicated upper respiratory tract infections in adults resolve spontaneously, although a small proportion become complicated by bacterial rhinosinusitis or bacterial pneumonia (particularly in high-risk patients with influenza, such as infants, elderly persons, and chronically ill patients). Symptoms caused by upper respiratory tract infection typically last 1 to 2 weeks, and most patients will feel much better within the first week. Sinusitis usually develops after an upper respiratory tract infection because of obstruction of the sinus ostia, whereas bacterial pneumonia in adults with influenza infection usually results from the effects of influenza on host immunity. Although most patients with the common cold exhibit sinus involvement on computed tomography performed within 2 to 4 days of symptom onset (14), only about 2% of cases of the common cold in adults are complicated by acute bacterial sinusitis (15). Bacterial rhinosinusitis should be suspected when symptoms have lasted at least 7 days and the illness is accompanied by purulent nasal discharge and other localizing features (16). As described below, antibiotic treatment of upper respiratory tract infection has not been shown to alter the rates of these uncommon complications.

*2.0 Recommendation 2. Antibiotic treatment of adults with nonspecific upper respiratory tract infection does not enhance illness resolution and is not recommended [A].* Studies specifically testing the effect of antibiotic treatment on complications of nonspecific upper respiratory tract infections have not been performed in adults. Life-threatening complications are rare.

2.1 Most randomized, placebo-controlled trials of antibiotic therapy for upper respiratory tract infections have been performed in children. A systematic review performed by the Cochrane Collaboration in 1998 evaluated trials in which patients with the diagnosis of up-

**Table. Randomized, Placebo-Controlled Trials of Antibiotic Treatment of Upper Respiratory Tract Infection in Adults**

| Study, Year (Reference)    | Location                | Participants   | Intervention  | Outcome  |
|----------------------------|-------------------------|--|---|--|
| Hoaglund et al., 1950 (18) | West Point, New York    | Male military recruits   | Placebo or aureomycin, 1–2 g/d  | Proportion of patients with cure or improvement at 24 hours: placebo, 45% (69 of 155); antibiotic, 44% (67 of 154)   |
| Howie and Clark, 1970 (19) | Glasgow, United Kingdom | Men 20–49 years of age with self-diagnosed “cold or flu-like illness”  | Placebo or dimethylchlorotetracycline, 300 mg twice daily for 5 days; treatment begun 2 days after illness onset if no improvement was seen | Proportion of illness episodes with purulent sputum: placebo ( <i>n</i> = 388), 41% vs. antibiotic ( <i>n</i> = 448), 40%; average days of purulent spit: 2.6 vs. 2.3 (results did not vary by cigarette smoking or age); average days of work lost: 1.5 vs. 1.1; no results were statistically significant ( <i>P</i> > 0.05) |
| Kaiser et al., 1996 (20)   | Switzerland             | Persons >16 years of age with common cold or upper respiratory tract infection, confirmed by clinician examination | Placebo or coamoxiclav, 375 mg three times daily for 5 days   | Proportion of patients with cure at day 5: placebo, 34% (48 of 142); antibiotic, 34% (49 of 146)   |

per respiratory tract infection or the common cold were treated with antibiotics or placebo (17). Trials in which 5% or more of participants had group A  $\beta$ -hemolytic streptococci on throat swab, those in which bronchitis was diagnosed, those in which patients had purulent sputum or purulent nasal discharge, and those in which symptoms lasted for more than 6 days were excluded. Analysis of seven trials including patients of all ages revealed that antibiotic treatment did not affect resolution of illness (summary odds ratio, 0.95 [95% CI, 0.70 to 1.28]) or loss of work time (measured in only one study). The three trials that enrolled adults only also showed no benefit of treating routine upper respiratory tract infections with antibiotics (Table) (18–20). In an additional randomized, controlled trial that compared penicillin with aspirin, no effect of antibiotic treatment was observed in hospitalized and ambulatory university students with nonspecific upper respiratory tract infection (21).

2.2 No published studies have specifically evaluated the effect of antibiotic treatment of upper respiratory tract infections on subsequent complications in adults. Among children, early antibiotic treatment of upper respiratory tract infection does not appear to prevent pneumonia or acute otitis media (22, 23). Systematic reviews by the Cochrane Collaboration report a consistent benefit of nasal decongestants in relieving nasal congestion associated with the common cold and equivocal results of treatment with zinc, echinacea, and humidified air

(24–27). Some of the variation in treatment effects of zinc and echinacea on cold symptoms in different trials may be due to variation in doses of active ingredient and formulations. A randomized, placebo-controlled trial of zinc acetate (28), published after the systematic review (25), reported a 3- to 4-day decrease in duration of illness and a decrease in illness severity. Study participants began treatment on the first day of illness onset and ingested an average of 6 lozenges, each containing 12.8 mg of zinc acetate, daily for 4 to 5 days.

3.0 Recommendation 3. *Purulent secretions from the nares or throat (commonly observed in patients with uncomplicated upper respiratory tract infection) predict neither bacterial infection nor benefit from antibiotic treatment [A].*

Although physicians often rely on the presence of purulent nasal discharge and purulent sputum to assign more specific diagnoses, such as acute rhinosinusitis or acute bronchitis, in patients with acute respiratory illness, these symptoms are also common in patients with upper respiratory tract infection. When not accompanied by additional predictors of bacterial rhinosinusitis (such as illness lasting  $\geq 7$  days), purulent nasal discharge and purulent sputum are weak predictors of bacterial infection in adults with upper respiratory tract infection. Purulence occurs when inflammatory cells or sloughed mucosal epithelial cells are present and can result from either viral or bacterial infection (20, 29, 30). Likewise, tonsillar exudate can result from either

viral or bacterial pharyngitis (31, 32). Placebo-controlled trials in patients with acute nasopharyngitis have found no difference in outcomes between patients with and without purulent nasal discharge (20). Other studies have also failed to find a clinical benefit of antibiotic treatment of adults with cough who had purulent sputum (33, 34).

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**Acknowledgments:** External review has included feedback from the Centers for Disease Control and Prevention; the American College of Physicians–American Society of Internal Medicine Clinical Efficacy Assessment Subcommittee; and representatives of the American Academy of Family Practitioners, the American College of Emergency Physicians, and the Infectious Diseases Society of America.

**Role of the Funding Source:** Partial support for the development of the Principles was provided by the Centers for Disease Control and Prevention, and final approval by the Centers for Disease Control and Prevention of all manuscripts submitted for publication was required.

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