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The Common Cold—Principles of Judicious Use of Antimicrobial Agents

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ABSTRACT. Most children will suffer between 3 and 8 colds per year, and over half of patients seen for the common cold are given an antimicrobial prescription. Unnecessary antimicrobial therapy can be avoided by recognizing the signs and symptoms that are part of the usual course of these diseases. Controlled trials of antimicrobial treatment of the common cold are reviewed. These trials consistently fail to show that treatment changes the course or outcome. Furthermore, antimicrobial therapy for patients with viral rhinosinusitis is not an effective way to prevent bacterial complications. Mucopurulent rhinitis (thick, opaque, or discolored nasal discharge) frequently accompanies the

common cold and is part of the natural course of viral rhinosinusitis. It is not an indication for antimicrobial treatment unless it persists without improvement for >10 to 14 days. *Pediatrics* 1998;101:181–184; common cold, upper respiratory tract infection, mucopurulent rhinitis, diagnosis, antimicrobial therapy.

ABBREVIATION. URI, upper respiratory tract infection.

PRINCIPLES

1. Antimicrobial agents should not be given for the common cold.
2. Mucopurulent rhinitis (thick, opaque, or discolored nasal discharge) frequently accompanies the common cold. It is not an indication for antimicrobial treatment unless it persists for >10 to 14 days.

BACKGROUND AND JUSTIFICATION

Recent evidence suggests that the common cold usually includes sinus disease.¹ Therefore, viral rhinosinusitis is used in this paper as a synonym for the common cold syndrome or nonspe-

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cific upper respiratory tract infection (URI). The acute illness typically is characterized by rhinorrhea, sore throat, cough, and fever. Because of the difficulty in defining criteria for this illness, the precise incidence of viral rhinosinusitis has been difficult to estimate. Most children will suffer between 3 and 8 colds per year; however, 10% to 15% of children will have at least 12 per year, particularly those attending day care centers.²⁻⁶ A review of Kentucky Medicaid claims found that 60% of patients seen for the common cold were given an antimicrobial prescription; that article estimated the annual cost of antimicrobial prescribing for the common cold in the United States at \$37.5 million.⁷ A recent survey in northern Virginia found that 71% of family practitioners and 53% of pediatricians would prescribe antimicrobials immediately for a 10-month-old infant with scant, green, mucopurulent nasal secretions of 1 day's duration.⁸

Rhinosinusitis and mucopurulent rhinitis are almost always caused by viral infections, for which antimicrobial use changes neither the course nor the outcome. Antimicrobial use is not only unnecessary but potentially harmful, because it increases the risk of colonization with resistant organisms and, thereby, heightens the chances that any subsequent invasive infection will be unresponsive to standard antimicrobial therapy.⁹

EVIDENCE SUPPORTING PRINCIPLES

Antimicrobial Agents Should Not Be Given for the Common Cold

Controlled trials of antimicrobial treatment of the common cold have consistently failed to show that treatment changes the course or outcome (Table). For example, a 1962 prospective, double-blind study of 781 children with colds demonstrated that 3.5% of those treated with antimicrobial agents developed purulent URI, compared with 2.6% of those treated symptomatically ($P = .5$).¹⁰ A more recent study of 261 children randomly treated with penicillin, tetracycline, or placebo showed similar results: 4.6% of the placebo group either did not improve or presented with evidence of a complication (eg, pneumonia) by 8 days, compared with 4.6% of the antimicrobial group ($P = 1$).¹¹

Two studies in adults showed modest benefits in those treated with antimicrobial agents and should be considered in evaluating the potential for benefit to children. The first, involving 212 adults with coughs or colds randomized to treatment with doxycycline or placebo, showed a reduction in the proportion with rhinorrhea at day 5 that was no longer apparent by day 10.¹² More recently, a trial of treatment with amoxicillin/clavulanate versus placebo among 314 adults with cold symptoms showed that antimicrobial treatment, although not beneficial

TABLE. Controlled Trials Assessing the Efficacy of Antibiotic Treatment for URI

Study (Year)	N	Comparison Groups	Outcome	Conclusion
Cronk et al ³³ (1954)	2177	PCN G and/or symptomatic treatment	Required return outpatient visit(s) PCN G 26%, symptomatic 20%	No difference between groups
Hardy et al ³⁴ (1956)	217	Abx* or placebo	Rate of all infectious complications abx 15%, placebo 15%	No difference between abx and placebo
Townsend ³⁵ (1960)	845	Abx† or symptomatic treatment	Rate of all infectious complications abx 14%, symptomatic 9%	No difference between abx and symptomatic
Townsend ¹⁰ (1962)	781	Abx† or symptomatic treatment	Rate of complications (eg, AOM) abx 3.5%, symptomatic 2.6%	No difference between abx and symptomatic
Lexomboon et al ¹¹ (1971)	261	PCN V or tetracycline or placebo	Not improved or complicated abx 5%, placebo 5%	No difference between abx and placebo
Gordon et al ³⁶ (1974)	89	Abx‡ or placebo	Improved symptoms or signs data not provided in publication	Abx do not change short-term course of URI
Stott and West ¹² (1976)	212	Doxycycline or placebo (adults only)	Runny nose at day 5 doxycycline 14%, placebo 30%	Doxycycline beneficial at day 5, not by day 10
Taylor et al ³⁷ (1977)	197	Amoxicillin, co-trimoxazole, or placebo	At day 8, purulent rhinitis: amoxicillin 6%, cotrimoxazole 4%, placebo 15%; at day 8, normal activity: amoxicillin 89%, cotrimoxazole 95%, placebo 97%	Marginal benefit from abx
Kaiser et al ¹³ (1996)	314	Coamoxiclav or placebo (adults, 61 with +nasopharyngeal cultures)	At day 5, for patients with +cultures: persistent/worse symptoms coamoxiclav 73%, placebo 96%;	Antibiotics may be indicated for a subset of adult patients, with sinusitis

Abbreviations: PCN indicates penicillin; abx, antibiotics; AOM, acute otitis media; coamoxiclav, amoxycillin/clavulanate.

* Three antibiotic groups: Gantrisin, Aureomycin, or penicillin.

† Four antibiotic groups: sulfonamides, tetracycline, penicillin, or chloramphenicol.

‡ Three antibiotic groups: ampicillin, penicillin, or erythromycin.

overall, was helpful at day 5 in a subgroup of patients with isolation of *Streptococcus pneumoniae*, *Moraxella catarrhalis*, or *Haemophilus influenzae* on a nasal swab.¹³ Given the modest benefit of antimicrobial agents even in these subgroups and the lack of benefit in most other studies (Table), antimicrobial agents are not indicated for treatment of viral rhinosinusitis.

The agents causing the common cold identified most commonly are rhinoviruses and coronaviruses, which together account for up to 60% of infections.^{2,14,15} Because these viruses are difficult to identify, they also may cause a substantial proportion of colds of unknown etiology. The etiologic agents of the common cold vary with host, age, and time of year. Each year in temperate climates, there are sequential outbreaks caused by different viruses, such as respiratory syncytial virus; influenza virus; coronavirus; rhinovirus; and parainfluenza 1, 2, and 3 viruses, interspersed with endemic infections caused by others, such as respiratory adenovirus. Occasionally, clinical findings may suggest a specific viral agent; some respiratory adenovirus infections (such as serotypes 3, 4, and 7) may present with pharyngitis and conjunctivitis, parainfluenza type 1 with croup, and influenza with prominent constitutional symptoms. More often, however, symptoms will be nonspecific and not characteristic of a specific agent.

The signs and symptoms associated with the common cold also may precede or accompany focal infections that are caused by bacteria. These infections, which include otitis media and bacterial sinusitis, should be diagnosed only when specific criteria are fulfilled.^{16–18} Unless clear evidence for the presence of a focal bacterial infection is present, the constellation of signs and symptoms associated with the common cold do not warrant treatment with antimicrobial agents.

Although a large majority of physicians realize that antimicrobial therapy will not hasten resolution of a cold, antimicrobials are often prescribed in an attempt to prevent bacterial complications. There are data that indicate that this is not an effective strategy. A recent metaanalysis of five randomized clinical trials of the efficacy of antimicrobial treatment of colds to prevent lower respiratory infections found no evidence for a protective effect.¹⁹ Although some studies suggest that intermittent antimicrobials begun at the onset of respiratory symptoms can help prevent acute otitis media in children at highest risk of recurrent disease,^{20,21} other studies do not.²² Furthermore, this approach is less effective than standard continuous prophylaxis, used for some high-risk children who meet stringent criteria,²³ when the two approaches are compared directly.²⁴

Other treatments are commonly used to treat the symptoms of the common cold, and although most show no benefit compared with placebo, some studies have shown efficacy for symptomatic treatments. For example, a controlled trial in adults of an antihistamine (clemastine fumarate) for treatment of experimental rhinovirus colds showed significant reductions in sneezing, rhinorrhea, and nasal secretions;²⁵ the reduction in symptoms may be larger than the marginal

benefit in symptoms demonstrated in certain subgroups by some antimicrobial trials. Therefore, if symptomatic relief is sought by patients, selected home remedies or preparations designed to treat symptoms may provide similar, although marginal, benefits without the risk of antimicrobial-resistant bacterial colonization or infection.

Mucopurulent rhinitis (thick, opaque, or discolored nasal discharge) frequently accompanies the common cold. It is not an indication for antimicrobial treatment unless it persists without improvement for >10 to 14 days.

Most episodes of viral rhinosinusitis follow a predictable course. Unnecessary antimicrobial therapy can be avoided by recognizing the signs and symptoms that are part of the usual course of this disease and thus are not suggestive of a secondary bacterial infection. Viral rhinosinusitis begins with the inoculation of virus onto the nasal, oral, or conjunctival mucosa, followed by infection of the local respiratory epithelium. The initial symptoms, which are caused both by cellular damage and by the inflammatory response, include nasal stuffiness and throat irritation. Within a few hours, sneezing and watery nasal discharge may occur, often accompanied by systemic complaints such as low-grade fever, malaise, headache, anorexia, and myalgias.²⁶ Cough occurs in 60% to 80% of viral rhinosinusitis^{15,27,28} and does not necessarily suggest a bacterial etiology. One to three days after the onset of illness, nasal secretions typically become thicker and more mucopurulent because they contain desquamated epithelial cells, polymorphonuclear cells, and bacteria that normally colonize the upper respiratory tract.²⁸ Physicians often differentiate mucopurulent rhinitis from viral rhinosinusitis; however, mucopurulent rhinitis is more appropriately considered part of the natural history of viral rhinosinusitis, not a distinct disease, and not an indication for antimicrobial therapy.^{29,30} The duration of illness usually ranges from 2 to 7 days. Although patients are generally improved by day 10, lingering symptoms, including cough (in up to 31% of patients) and nasal discharge (35%), can persist in children and adolescents for >2 weeks.^{28,31} With an average of six respiratory tract infections per year, and more if children are in day care,^{2–6} many children will have sequential episodes of viral rhinosinusitis with little time for improvement between episodes.

In 1984, Todd³² randomized 142 children with mucopurulent nasopharyngitis into groups that received either antimicrobials (cephalexin), symptomatic therapy, or placebo. Although bacteria often were identified in nasal secretions, antimicrobial treatment did not reduce the number of potentially pathogenic organisms obtained from nasopharyngeal cultures. Additionally, no differences in clinical outcomes between antimicrobial and placebo-treated groups were found at 5 to 6 days, based on both physician and parent assessments. Of the children treated with antimicrobials, 76% had continued nasal discharge, compared with 63% of those treated with placebo ($P = .1$); 7% had evidence of complications, compared with 8% of those treated with placebo

($P = .9$); and 35% reported clinical improvement, compared with 31% of those treated with placebo ($P = .6$).

Thus, mucopurulent rhinitis is part of the natural course of viral rhinosinusitis, and there is no good evidence that children with this syndrome benefit from treatment with antimicrobials unless symptoms persist for 10 to 14 days without improvement. The recent emergence of resistant pneumococci, together with evidence that children on antimicrobials are at increased risk, suggests that antimicrobials should be withheld from patients with colds accompanied by mucopurulent rhinitis.

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