

Cough Illness/Bronchitis—Principles of Judicious Use of Antimicrobial Agents

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ABSTRACT. Millions of courses of antibiotics are prescribed for children with acute cough illness each year, despite evidence from randomized, placebo-controlled trials that such treatment is not effective. Evidence that children with cough for ≤ 10 days should not be treated with antimicrobial agents is presented. Older children with prolonged cough or those with underlying lung disease may benefit from antimicrobial treatment directed specifically at *B pertussis*, *M pneumoniae*, *C pneumoniae*, *P aeruginosa*, or other specific infections. None of the routinely prescribed cephalosporin or amino penicillin antimicrobials would be effective for these organisms. Noninfectious diagnosis should be sought in children with markedly prolonged cough. *Pediatrics* 1998; 101:178–181; *bronchitis, cough, diagnosis, antimicrobial therapy, antimicrobial resistance, pediatrics.*

ABBREVIATION. NP, nasopharyngeal.

PRINCIPLES

1. Regardless of duration, nonspecific cough illness/bronchitis in children rarely warrants antimicrobial treatment.
2. Antimicrobial treatment for prolonged cough (>10 days) may be indicated occasionally. Pertussis should be treated according to established recommendations. *Mycoplasma pneumoniae* infection may cause pneumonia and prolonged cough (usually in children >5 years of age); a macrolide agent (or tetracycline for children ≥ 8 years of age) may be used for treatment. Children with underlying chronic pulmonary disease (not including asthma) may benefit occasionally from antimicrobial therapy for acute exacerbations.

BACKGROUND AND JUSTIFICATION

Bronchitis is technically defined as inflammation of the bronchial respiratory mucosa, resulting in productive cough. The clinical definition of bronchitis in children is not well established, but most clinicians who make the diagnosis do so for a child with cough, with or without fever or sputum production.

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Although the term bronchitis does not imply any specific etiology and studies demonstrate that this self-resolving illness is most commonly caused by viral pathogens,^{1–3} in practice, a diagnosis of bronchitis often results in a prescription for an antimicrobial agent, reflecting the belief that bacteria cause this illness. Millions of antibiotic courses are prescribed each year for children diagnosed with bronchitis. In a study of 1398 outpatient visits of children <14 years old with a chief complaint of cough, bronchitis was diagnosed in 33% of cases, and 88% of these children were prescribed an antimicrobial.⁴

Because the pathologic definition of bronchitis as inflammation of the bronchi does not reflect the term's clinical usage, imply the need for antimicrobial therapy, or imply a specific etiology, the diagnosis and management of cough illness in children will be reviewed here using the term cough illness/bronchitis. This term excludes more specific diagnoses such as pneumonia, bronchiolitis, and asthma.

A variety of terms are used in the literature to describe conditions marked by cough, including bronchitis, wheezy bronchitis, tracheobronchitis, and asthmatic bronchitis. The lack of consensus regarding nomenclature and clinical definitions of cough illnesses leads to difficulty comparing patient populations and results from studies of cough illness/bronchitis. The lack of a standardized case definition, the difficulty of obtaining appropriate specimens for viral and bacterial diagnostic tests, the high rate of spontaneous resolution of illness, and the lack of placebo-controlled treatment trials for pediatric cough illness/bronchitis all undermine the establishment of a firm consensus on diagnosis and treatment. However, studies among adolescent and adult patients, together with the few pediatric studies of cough illness, provide important information about the treatment and natural history of cough illness/bronchitis that can be applied to children. Despite the need for additional research, information is sufficient to provide principles that can be used to limit unnecessary use of antimicrobial agents for treatment of this condition.

EVIDENCE SUPPORTING PRINCIPLES

Regardless of Duration, Nonspecific Cough Illness/Bronchitis in Children Rarely Warrants Antimicrobial Treatment

Seven randomized, placebo-controlled antibiotic trials for bronchitis among adult patients have been pub-

lished in the English language, peer-reviewed medical literature. A metaanalysis that included six of these studies concluded that there is no evidence to support the use of antibiotic treatment for acute bronchitis.⁵ Three trials that used erythromycin, doxycycline, or trimethoprim/sulfamethoxazole demonstrated minimal improvement in duration of cough and time lost from work in the group treated with antibiotics.⁶⁻⁸ The remaining four trials, including the two that the authors concluded best fulfilled criteria for methodologic soundness, showed no difference in outcomes between those who received placebo and those treated with erythromycin, doxycycline, or tetracycline.⁹⁻¹²

There are no randomized, placebo-controlled antibiotic trials of children with cough illness/bronchitis strictly defined by sputum production; however, several pediatric studies have evaluated the use of antibiotics for cough illnesses, which in common practice are called bronchitis and are treated with antibiotics.¹³⁻¹⁶ None of these studies showed any benefit of antibiotic use for the cough.

Although most practitioners recognize that the majority of cough illness results from viral infections, some believe that lower respiratory bacterial superinfections might be averted by prophylactic use of antimicrobial agents. At least nine trials have evaluated the role of antibiotic treatment for preventing bacterial complications of viral respiratory illnesses. A metaanalysis of these trials concluded that antibiotics did not prevent or decrease the severity of bacterial complications subsequent to viral respiratory tract infections.¹⁷

The lack of benefit from antimicrobial therapy is consistent with community- and hospital-based studies in the United States and other areas of the world that implicate nonbacterial organisms as the etiologic agents of cough illness/bronchitis. These studies demonstrate that viral pathogens such as parainfluenza virus, respiratory syncytial virus, and influenza virus account for the majority of agents identified among children with cough illness/bronchitis.^{1,2,18,19} Among children >5 years, *Mycoplasma pneumoniae* was also recognized to cause cough illness/bronchitis.¹ Recently, *Chlamydia pneumoniae* has also been isolated from children with nonspecific cough illness.²⁰ Taken together, there is ample evidence that cough illness/bronchitis in children is primarily caused by viral pathogens or, in the case of older children, sometimes by *M pneumoniae* or *C pneumoniae*. There is little if any microbiologic evidence for an important role of other pathogenic bacteria in the etiology of cough illness/bronchitis.

Unequivocally establishing the etiology of cough illness/bronchitis is difficult, because obtaining secretions directly from the bronchi of children with this syndrome is an invasive procedure and seldom done. Neither the character nor the culture results of surrogate specimens such as sputum (defined by the presence of fewer than 10 epithelial cells per high-power field) or nasopharyngeal (NP) secretions is sufficiently predictive of a bacterial infection of the bronchi to be of use in defining the need for antimicrobial therapy. Sputum, comprising epithelial cells, polymorphonuclear lymphocytes, and noncellular

elements, is a nonspecific response to airway inflammation, produced in response to both viral and bacterial infections as well as to noninfectious processes. In a study of 72 acute episodes of wheezy bronchitis among 22 children 5 to 15 years of age, only 17% of sputum samples contained a potentially pathogenic bacterium, and in half of these samples, a viral pathogen also was isolated.²¹ Leukocytes were found in 82% of virus-positive sputum specimens and in 85% of bacteria-positive specimens. Thus, in the absence of physical signs of pneumonia, neither the production of sputum nor the character of sputum is predictive of a bacterial etiology for cough. The presence of bacteria in a culture of NP secretions also should not be used as an indication that cough may be caused by a bacterial pathogen. Studies have evaluated the use of NP cultures to predict the causative organism of other upper and lower respiratory tract infections, such as otitis media, sinusitis, and pneumonia, for which there are accepted standard methods for obtaining specimens directly from the site of infection.²²⁻²⁵ Simultaneous cultures of the nasopharynx and middle ear fluid,²² maxillary sinus fluid,²⁴ or percutaneous lung aspiration specimens²⁵ demonstrated that NP cultures were poor predictors of the true bacterial pathogens. By analogy, it can be surmised that NP cultures are not likely to be useful in predicting the presence of bacteria in the bronchi. Finally, it should be noted that the mere presence of bacteria at the level of the bronchi, even if there were practical means to collect such specimens, may not reflect true infection of the bronchial mucosa.

Some practitioners use the presence of fever in conjunction with cough to diagnose bronchitis and prescribe antibiotic treatment.⁴ However, fever is an expected component of cough illness/bronchitis and does not indicate that cough is related to a bacterial infection or that any benefit would be derived from antimicrobial therapy. In studies of experimentally and naturally induced viral respiratory infections, fever was found to be a common sign, especially in the first 2 days of illness, which resolved over the ensuing few days.²⁶⁻²⁹

Antimicrobial Treatment for Prolonged Cough (>10 Days) Occasionally May Be Indicated

Pertussis should be treated according to established recommendations. *Mycoplasma pneumoniae* infection may cause pneumonia and prolonged cough (usually in children >5 years of age); a macrolide agent (or tetracycline for children ≥ 8 years of age) may be used for treatment. Children with underlying chronic pulmonary disease (not including asthma) occasionally may benefit from antimicrobial therapy for acute exacerbations.

The majority of prolonged cough illnesses are allergic, postinfectious, or viral in nature and do not require antibiotic therapy. Reactive airway disease has been recognized recently as one of the most common causes of recurrent or prolonged cough among children.³⁰ These children may have minimal or no appreciable wheezing on physical examination but may respond dramatically to bronchodilator therapy, with resolution of cough and documented

improvement in airway reactivity.³⁰⁻³³ Because bronchospasm is commonly triggered by an acute viral respiratory infection, these children require treatment for relief of bronchospasm, not antibiotics.

Careful studies of experimentally induced and culture-confirmed rhinovirus colds in adults have documented that cough persists after fever, myalgia, sneezing, and sore throat have resolved.^{27,29,34} In fact, 20% of subjects continue to cough ≥ 14 days after onset of symptoms.²⁹ A clear understanding that prolonged cough is an expected part of uncomplicated viral upper respiratory tract infection and does not itself indicate a bacterial infection of the bronchi or the sinuses should help practitioners and patients avoid a large burden of unnecessary antibiotic use.

Prolonged cough caused by other specific pathogens may benefit from antimicrobial treatment and should be considered in the differential diagnosis of prolonged cough. Pertussis classically causes paroxysms of cough followed by a characteristic inspiratory whoop. Particularly among older children and adults, pertussis also can present with a prolonged cough and no whoop. In a study of 130 university students with cough for ≥ 6 days, 26% were found to have culture or serology evidence of a recent *Bordetella pertussis* infection.³⁵ Treatment with erythromycin, if started early in the course of disease, may decrease the duration of symptoms. However, if started later in disease, treatment with erythromycin may only diminish communicability of *B pertussis*, but is of no value in hastening resolution of the cough.³⁶ A diagnosis of pertussis can be confirmed by culture of the organism or antigen detection from NP secretions in the acute phase or serologic diagnosis in the later phases of the illness.

Although *M pneumoniae* infections may occur in young children, they are more likely to be mild, nonpneumonic infections than those in school children and adolescents, which may cause pneumonia and prolonged respiratory illness with cough.³⁷⁻³⁹ Specific antimicrobial therapy may be of benefit in decreasing communicability and shortening the duration of illness, although the effect on the latter is small.^{40,41} There are no specific or pathognomonic signs of cough caused by *M pneumoniae* infection. Therefore, treatment should not be given unless the cough illness is prolonged or pneumonia is documented. Laboratory confirmation of the diagnosis is usually made by acute- and convalescent-phase serologic testing.⁴² When treatment is elected, a macrolide antimicrobial agent or tetracycline for children ≥ 8 years of age should be used.

Diagnosis and management of cough illness/bronchitis in children with underlying chronic pulmonary disease must take into consideration differences in epidemiology, natural history, and pathogenesis. Children with cystic fibrosis may benefit from antimicrobial therapy directed at *Pseudomonas aeruginosa*, *Staphylococcus aureus*, or *Haemophilus influenzae* during episodes characterized by cough, increased secretions, rales, rhonchi, and fever.⁴³ Similarly, children with other underlying severe chronic lung diseases (eg, bronchopulmonary dysplasia, lung hypoplasia, ciliary dyskinesia, chronic aspiration) may be more likely to benefit from

antibiotic treatment because of increased likelihood of bacterial colonization, impaired pulmonary clearance mechanisms, or immune compromise. Treatment must be tailored for each child; general principles of judicious antimicrobial use are particularly appropriate for these children to decrease the adverse effects from multiple courses of antibiotics and resultant colonization with antibiotic-resistant organisms.

Children with markedly prolonged cough (4 to 8 weeks) should be investigated for possibly treatable causes, including reactive airway disease, tuberculosis, foreign body aspiration, pertussis, cystic fibrosis, or sinusitis. If possible, empiric antimicrobial therapy should be avoided in the initial management of a prolonged cough; rather, a specific diagnosis should be sought.

The practice of restricting antibiotic use to a small subset of prolonged cough illnesses is supported by the medical literature. Standard pamphlets or letters explaining the nature of the illness may facilitate the return to day care or school of a child with a viral respiratory infection or allergy-induced cough who is otherwise well. The cost of a follow-up visit for those few children whose illness is not improving over time should be balanced against the high likelihood of spontaneous resolution of the coughing illness without antibiotic therapy and the risk to the child and the community of unnecessary antibiotic use.

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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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