Approximately three quarters of all outpatient antibiotics are prescribed for either upper respiratory tract infections (URIs) or bronchitis [1]. Antibiotic utilization rates are highest among children. Effective management of these infections has become more difficult because of the emergence of pathogens increasingly resistant to antimicrobial agents. Recent publications have provided guidance for judicious use of antibiotics for pediatric URIs [2,3] (Table). These principles stress that accurate diagnosis should be based on clinical manifestations and the use of laboratory testing when indicated. Since many infections are treated empirically, one must be knowledgeable about both the organisms likely to cause the infection and the expected antibiotic susceptibilities. Therapy should both eradicate the infecting organism and be effective in preventing any complications. The natural history of these infections needs to be understood because many infections will not require treatment with antibiotics. Curtailing unnecessary antibiotic use would protect both patients and the community from increasing bacterial antibiotic resistance. This paper will review current recommendations for the use of antimicrobial agents in 4 common pediatric conditions: acute otitis media (AOM), pharyngitis, sinusitis, and the common cold.

Common Cold
The average child has 3 to 8 colds per year [4,5]. The clinical syndrome is caused by various viral pathogens, including rhinoviruses that can account for 30% to 50% of all cases and 80% of cases during fall epidemics [6,7]. Other viral agents include respiratory syncytial virus, coronavirus, parainfluenza virus, and influenza virus. Despite the predominance of viral agents causing the common cold, antibiotics continue to be prescribed frequently in managing patients. In a survey performed among clinicians in Kentucky, 60% of patients with colds were given antibiotics [8].

Rhinovirus infections occur year-round and will regularly affect most individuals [9]. Viral activation of host inflammatory pathways and involvement of mucosal parasympathetic neural systems result in the well-known clinical manifestations of nasal obstruction, mucopurulent rhinitis, sneezing, and scratchy throat; some individuals also develop a cough. Purulence develops in nasal secretions due to an influx of neutrophils into the inflamed mucosa [7]. Contrary to the belief of patients and many physicians, a change in the color or characteristics of the nasal discharge is not a reliable sign of bacterial infection [10,11]. Typically, most individuals improve after 1 week, although 25% will have symptoms lasting 2 weeks. While colds are associated with little morbidity, complications can include otitis media, sinusitis, and exacerbations of reactive airway disease.

Studies have demonstrated the lack of efficacy of antibiotics on the course of the common cold [12]. While not systematically investigated, available evidence suggests that antibiotics neither alter the clinical course nor prevent complications of the common cold. A meta-analysis of randomized controlled trials carried out in different clinical settings demonstrated that antibiotic treatment of children with non-specific URI symptoms neither shortened the duration of illness nor prevented the development of secondary bacterial pneumonia [13]. Nevertheless, many physicians continue to prescribe antibiotics within 24 to 48 hours of onset of mucopurulent rhinitis in infants [14]. Thick, opaque, or discolored nasal discharge frequently occurs in patients with the common cold, and it is not an indication for antibiotic treatment unless it persists beyond 10 to 14 days, which suggests possible sinusitis.

While conventional symptomatic therapies, including antihistamines and adrenergic agents, do not prevent the spread of infection, decrease duration of symptoms, or diminish complications, such treatments have consistent, if only modest, effects on common cold symptoms [7]. Antibiotic therapy for the common cold is not warranted.

Acute Otitis Media
AOM is one of the most common diseases of childhood. The peak incidence of AOM is in the first 2 years of life, with most cases occurring between 6 and 12 months [15]. Eighty percent of children experience 1 episode of AOM in the first year of life [16,17]. Risk factors for the development and persistence of otitis media in children include low socioeconomic status,
Acute otitis media
Episodes of otitis media should be classified as acute otitis media (AOM) or otitis media with effusion (OME).
Antimicrobial agents are indicated for treatment of AOM; however, diagnosis requires documented middle ear effusion AND signs or symptoms of acute local or systemic illness.
Acute otitis media can be treated with a 5- to 7-day course of antimicrobial agents in certain children 2 years of age and older. Younger children and children with underlying medical conditions, craniofacial anomalies, chronic or recurrent otitis media, or perforation of the tympanic membrane should be treated with a standard 10-day course.
Persistent middle ear effusion (OME) for 2 to 3 months after therapy for AOM is expected and does not require retreatment.
Antimicrobial agents are not indicated for initial treatment of OME; treatment may be indicated if effusions persist for 3 months or more.
Antimicrobial prophylaxis should be reserved for control of recurrent AOM, defined as ≥ 3 distinct and well-documented episodes per 6 months or ≥ 4 episodes per 12 months.

Pharyngitis
Diagnosis of group A streptococcal pharyngitis should be made based on the appropriate laboratory test results in conjunction with clinical and epidemiologic findings.
Antimicrobial therapy should not be given to a child with pharyngitis in the absence of identified group A streptococci or another bacterial pathogen known to cause pharyngitis. If presumptive therapy is given for group A streptococcal pharyngitis, it should be discontinued if the pharyngeal culture is negative for this organism.
Penicillin remains the drug of choice for treating group A streptococcal pharyngitis.

Acute sinusitis
Clinical diagnosis of bacterial sinusitis requires the following: nasal discharge and daytime cough without improvement for 10 to 14 days, or more severe signs and symptoms of acute sinusitis (eg, temperature of 39°C (102°F) or higher, facial swelling, facial pain).
The common cold is a rhinosinusitis that often includes radiologic evidence of sinus involvement; radiographs, therefore, should be used only in selected circumstances and should be interpreted with caution. Radiographs may be indicated when episodes of sinusitis are recurrent, when complications are suspected, or when the diagnosis is unclear.
Initial antimicrobial treatment of acute sinusitis should be with the agent with the narrowest spectrum that is active against the likely pathogens.

concentration (MIC). Clinical relevance lies in comparing the bacterial MIC with antibiotic levels achievable at the site of infection [22]. Concentrations of a β-lactam antibiotic in the middle ear fluid above the MIC can eradicate intermediate-resistant and some resistant pneumococci. The risk for infection with penicillin-nonsusceptible pneumococci is highest in children recently treated with antibiotics, those with recurrent episodes of AOM, children under the age of 2 years, and those attending child care centers [23].

The majority of uncomplicated cases of AOM resolve spontaneously [24]. Through utilization of repeat tympanocenteses (double tap), pneumococcal infections are noted to resolve in 20% of untreated children with AOM. Second aspirates in AOM caused by *H. influenzae* and *M. catarrhalis* are sterile in about 50% of cases [25]. It is estimated that 70% to 90% of AOM episodes resolve without therapy within a 7- to 14-day period [26]. The cumulative evidence from randomized controlled trials comparing antibiotic therapy with placebo in children with AOM favors antibiotics, although the therapeutic benefit is limited [27–30]. Treatment likely shortens the period of fever and discomfort. The incidence of complications following AOM is very low today [29].

For a first or sporadic episode of AOM, amoxicillin is the first-choice drug. This antibiotic has a long record of both safety and clinical efficacy in treating patients with AOM. It has a narrow spectrum of activity, and, depending on the dose administered, the antibiotic concentration in the middle ear fluid is effective in eradicating most penicillin-nonsusceptible pneumococci. A consensus panel convened by the Centers for Disease Control and Prevention has formulated treatment recommendations for children with AOM [25] (Figure 1). As recommended, high-dose amoxicillin (70 to 90 mg/kg/day) should result in middle ear fluid antibiotic concentrations effective against two thirds of intermediate-resistant and one third of resistant pneumococcal strains [31,32]. Treatment of AOM in children who have either recently received antibiotics or who have had treatment failures (ie, clearly not improved, continued fever and/or discomfort) involves therapy with

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**Figure 1.** Treatment recommendations for children with acute otitis media (AOM). IM = intramuscular. *High dose amoxicillin, 80–90 mg/kg/day. High dose amoxicillin-clavulanate, 80–90 mg/kg/day of the amoxicillin component should utilize 14:1 amoxicillin-clavulanate preparation. †Efficacy is documented in AOM treatment failures when 3 daily doses are used. ‡Indicated if *S. pneumoniae* is known to be causative organism. Clindamycin is not effective against *H. influenzae* or *M. catarrhalis.* (Adapted with permission from Dowell JF, Butler JC, Giebink GS. Acute otitis media: management and surveillance in an era of pneumococcal resistance—a report from the Drug-resistant *Streptococcus pneumoniae* Therapeutic Working Group. Pediatr Infect Dis J 1999;18:1–9.)
medications effective against both β-lactamase–producing organisms and drug-resistant S. pneumoniae. Medications recommended by the consensus panel are those for which strong evidence for efficacy exists. While many antibiotics are available to treat AOM [22], a recent review found no evidence to support any particular antibiotic regimen as more effective than another in relieving the symptoms of AOM [30].

A 10-day course of therapy is indicated for AOM in children younger than 2 years of age. Ten days of treatment is also warranted in patients with a perforated tympanic membrane, chronic or recurrent otitis media, children with craniofacial anomalies, and in immunocompromised individuals [32]. A 5- to 7-day course of therapy is appropriate for children 2 years of age or older with uncomplicated presentations [33].

**Pharyngitis**

Pharyngitis is one of the most prevalent infections among children and adolescents. Viral agents cause most episodes of pharyngitis. *Streptococcus pyogenes*, also known as group A β-hemolytic streptococcus (GABHS), is the leading bacterial cause of pharyngitis in the pediatric population, accounting for 15% to 50% of cases [34]. GABHS infections occur most commonly in 5- to 15-year-olds and are uncommon in children younger than 3 years old. Infections occur year-round but increase during the school year. The clinical diagnosis of pharyngitis caused by GABHS can be challenging. Even the "classic" symptoms of acute onset of sore throat, dysphagia, fever, headache, malaise, and abdominal pain are neither sensitive nor specific for GABHS pharyngitis. Bacterial colonization of the pharynx with GABHS can occur without causing symptoms, a finding in 15% to 20% of schoolchildren [35]. The GABHS carrier state is a relatively benign condition to both the carriers and their contacts. A properly performed and interpreted throat culture remains the standard for the documentation of GABHS in the upper respiratory tract and for the confirmation of the clinical diagnosis of acute streptococcal pharyngitis. While highly sensitive, definitive results from throat cultures may take 24 to 48 hours. The delay in both diagnosis and subsequent therapy may be avoided through use of rapid antigen-detection tests, enzyme immunoassays that can confirm the presence of GABHS carbohydrate on a throat swab in a matter of minutes [36]. Being very highly specific (greater than 95%) when compared with blood agar cultures, a positive rapid test can be considered the equivalent of a positive throat culture. Rapid tests, however, are less sensitive. Studies have demonstrated that a large proportion of patients with false-negative rapid tests are infected with GABHS and are not merely streptococcal carriers. Newer tests, such as the optical immunoassay, may increase assay sensitivity. Currently, advisory committees recommend that while either a positive throat culture or rapid test confirms the presence of GABHS, a negative rapid streptococcal test should be confirmed with a throat culture [37].

GABHS pharyngitis is typically a self-limited illness lasting 3 to 5 days [38]. Because untreated patients are at risk for developing acute rheumatic fever, once the diagnosis of GABHS is made by antigen detection or throat culture, antibiotic therapy is essential [39]. Additionally, antibiotics may prevent supplicative complications, more rapidly resolve the illness, and prevent the spread of GABHS infection.

A guiding principle in the management of patients with GABHS pharyngitis is the need to eradicate the organism from the pharynx. While many antimicrobial agents can eliminate GABHS from the infected patient’s pharynx [40], only treatment with intramuscular penicillin has been demonstrated to prevent acute rheumatic fever [41]. Because of the comparable eradication rates of intramuscular and oral penicillin, American Heart Association guidelines recommend 10 days of oral penicillin V as the treatment of choice for GABHS pharyngitis. The American Academy of Pediatrics adds that oral penicillin V can be given 2 to 3 times daily for 10 days [42]. Over many decades, GABHS remain susceptible to penicillin [43].

Both once-daily antibiotic dosing and shortened treatment duration for GABHS pharyngitis have been studied. Once-daily oral penicillin V does not appear to be effective in eradicating GABHS from the throat [44]. Recent studies, however, have demonstrated that some cephalosporin antibiotics (cefadroxil, cefixime, cefitobuten, cefpodoxime, cefdinir) and azithromycin are comparable to treatment with penicillin given 3 to 4 times a day in eradicating GABHS from the throat [40,45]. When compared to treatment with penicillin, microbiologic cure rates appear slightly higher in children treated with cephalosporins. However, these rates may represent greater effectiveness of the cephalosporins in eliminating GABHS in carriers rather than improved outcomes in infected children [46]. Once-daily amoxicillin has been demonstrated to be as effective as 3- to 4-times daily oral penicillin V in treating GABHS pharyngitis [47,48]. Attempts to reduce the total duration of therapy with oral penicillin V in GABHS pharyngitis have not proven successful [49,50]. Several cephalosporins have been shown to be effective in bacterial eradication when used for less than 10 days [51–53]. Studies evaluating short-course treatment with azithromycin have had variable results [54,55].

Given its safety, low cost, and narrow spectrum, oral penicillin V for 10 days remains the drug of first choice for GABHS pharyngitis. A single dose of intramuscular benzathine penicillin is effective. Future studies might confirm that once-daily amoxicillin for 10 days may an acceptable alternative treatment regimen. Penicillin-allergic patients should receive erythromycin.
Acute Bacterial Sinusitis

Acute bacterial sinusitis (ABS) is seen frequently in the primary care setting and is the fifth most common diagnosis for which antibiotics are prescribed [56]. Many conditions affecting the upper respiratory tract, particularly the common cold, can confound the diagnosis of ABS. Inflammatory processes in the nose or paranasal sinuses, from viral infection or allergic rhinitis, can result in both ciliary dysfunction and obstruction of the sinus ostia. The negative pressure in a closed sinus cavity, when combined with sneezing and sniffing, facilitates bacterial access into the sinus [57]. It is estimated that 5% to 10% of viral URIs are complicated by ABS [58].

Approximately 60% of patients with the clinical diagnosis of ABS will have bacteria identified after sinus puncture [59]. *S. pneumoniae* (42%), *H. influenzae* (21%), and *M. catarrhalis* (20%) account for the majority of microbiologically...
confirmed cases of pediatric ABS. While *H. influenzae* and *M. catarrhalis* cannot be ignored, empiric therapy must adequately address antibiotic resistance in the more pathogenic *S. pneumoniae*. Risk factors for infection with penicillin-nonsusceptible pneumococci include prior antibiotic utilization (< 30 days), age younger than 2 years, attendance at child care centers, and exposure to tobacco smoke [59,60]. In determining the optimal antibiotic regimen to eradicate these pathogens, it is important to note that 50% of children with microbiologically confirmed ABS and 65% of all untreated children with ABS will likely have spontaneous resolution without antibiotic therapy [59].

Management of ABS depends on clinical acumen, which allows for the identification of children with upper respiratory symptoms who will benefit from antibiotic therapy. Since no sign or symptom is specific for the diagnosis of ABS, a clinical diagnosis is best made in the presence of a collection of findings. While not always easily done, children with ABS can be classified according to severity of illness. In that most children with viral URIs are asymptomatic by 10 days, mild ABS is characterized by persistence of upper respiratory symptoms for greater than 10 days without improvement. These symptoms include nasal congestion and discharge of abnormal quality or color, daytime cough, and cough that is persistent at night [57]. Moderate ABS is characterized by upper respiratory symptoms lasting more than 10 days in a child with low-grade fever and unilateral maxillary or frontal tenderness. A toxic-appearing, febrile child who may have the above symptoms for even less than 10 days can be classified as having severe ABS [57,60].

As abnormalities of the paranasal sinuses are commonly found on conventional radiographs and computed tomography scans of patients with viral URIs, routine radiographic studies are neither helpful nor necessary in the management of the child with uncomplicated ABS [61]. However, radiographic evaluations and consultation with subspecialists are typically indicated in the management of some children with severe ABS and those with orbital or intracranial complications.

Antibiotic treatment of the patient with ABS is based on the severity of illness and the likelihood of infection with resistant pathogens [59–62]. Children with mild to moderate ABS who have not received antibiotics in the previous 4 to 6 weeks should receive amoxicillin (45 to 90 mg/kg/day). Alternative antibiotics might include cefpodoxime proxetil, cefuroxime axetil, or cefdinir. In children with type I allergy to *S. pneumoniae* and *H. influenzae*, alternative antibiotics include penicillin-lactam plus *S. pneumoniae* coverage (eg, clindamycin or azithromycin). These latter antibiotics, along with *S. pneumoniae* plus *M. catarrhalis* coverage (eg, amoxicillin-clavulanate), are recommended in the management of some children with severe disease who will benefit from antibiotic therapy (Figure 2).

**Conclusion**

Current recommendations for the management of upper respiratory infections in children provide a sound approach to the need for antibiotic therapy in the patient, reduction of unnecessary use of antimicrobial agents in nonbacterial infections, and the appropriate use of antibiotics when bacterial disease is likely. Rational use of antibiotic therapy for these infections will also result in the protection from infections with resistant bacteria. This approach to management benefits both patients and society.

Corresponding author: Sherman J. Alter, MD, Department of Pediatrics, The Children’s Medical Center, 1 Children’s Plaza, Dayton, OH 45404-1815, sherman.alter@wright.edu.

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**References**


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