

# Antibiotic Use in Acute Upper Respiratory Tract Infections

ROGER ZOOROB, MD, MPH; MOHAMAD A. SIDANI, MD, MS; RICHARD D. FREMONT, MD; and COURTNEY KIHLEBERG, MD, MSPH, *Meharry Medical College, Nashville, Tennessee*

Upper respiratory tract infections account for millions of visits to family physicians each year in the United States. Although warranted in some cases, antibiotics are greatly overused. This article outlines the guidelines and indications for appropriate antibiotic use for common upper respiratory infections. Early antibiotic treatment may be indicated in patients with acute otitis media, group A beta-hemolytic streptococcal pharyngitis, epiglottitis, or bronchitis caused by pertussis. Persistent cases of rhinosinusitis may necessitate the use of antibiotics if symptoms persist beyond a period of observation. Antibiotics should not be considered in patients with the common cold or laryngitis. Judicious, evidence-based use of antibiotics will help contain costs and prevent adverse effects and drug resistance. (*Am Fam Physician.* 2012;86(9):817-822. Copyright © 2012 American Academy of Family Physicians.)



► **Patient information:** A handout on antibiotic use is available online at <http://familydoctor.org/familydoctor/en/drugs-procedures-devices/prescription-medicines/antibiotics-when-they-can-and-cant-help.html>.

► **See related editorial on page 810.**

Upper respiratory tract infections (URIs) are commonly treated in family physicians' practices. Uncomplicated URIs account for 25 million visits to family physicians and about 20 to 22 million days of absence from work or school each year in the United States.<sup>1</sup> Despite the majority of these infections being viral, a high percentage are treated with antibiotics<sup>2</sup> (*Table 1*<sup>3-18</sup>). A study from a large, outpatient ambulatory network of more than 52,000 cases of URI showed that antibiotics were prescribed in 65 percent of patients.<sup>19</sup> Overuse of antibiotics may lead to resistance, increased cost, and increased incidence of adverse effects, including anaphylaxis.<sup>20</sup>

## Common Cold

The common cold is a mild, self-limited URI with symptoms of runny nose, sore throat, cough, sneezing, and nasal congestion. It is a heterogeneous group of viral diseases, and therefore does not respond to antibiotics.<sup>1,21</sup> Between 1991 and 1999, the rate of overall antibiotic use for URIs decreased in the United States. However, the use of

broad-spectrum antibiotics increased.<sup>22</sup> One study reviewed randomized controlled trials (RCTs) from 1966 to 2009 that compared antibiotic therapy with placebo in persons who had symptoms of acute URI of less than seven days' duration, or acute purulent rhinitis of less than 10 days' duration.<sup>11</sup> The authors found insufficient evidence to recommend antibiotics for the treatment of purulent or clear rhinitis in children or adults.

## Influenza

Influenza is an acute URI caused by influenza virus A or B. It affects patients of all ages, but the highest incidence is in children. Adults older than 65 years and children younger than two years have the highest mortality rates from influenza.<sup>23,24</sup> Vaccination is the mainstay of prevention. Supportive care is the foundation of treatment, but antiviral therapy, such as the neuraminidase inhibitors oseltamivir (Tamiflu) and zanamivir (Relenza), may decrease the duration of the illness by one day if started within 48 hours of symptom onset.<sup>16,17</sup> The Centers for Disease Control and Prevention no longer recommends the use of amantadine for influenza therapy.<sup>24</sup>

## SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	References
Amoxicillin is the preferred treatment in patients with acute bacterial rhinosinusitis.	C	10
Short-course antibiotic therapy (median of five days' duration) is as effective as longer-course treatment (median of 10 days' duration) in patients with acute, uncomplicated bacterial rhinosinusitis.	B	31
Antibiotic therapy should be considered for children six to 35 months of age with acute otitis media.	B	37, 38
Antibiotics should not be used in patients who have otitis media with effusion.	C	43
Penicillin should be used in patients with streptococcal pharyngitis to decrease the risk of rheumatic fever, alleviate symptoms, and decrease communicability.	B	45, 46, 49, 52
Antibiotics should not be prescribed for acute laryngitis.	A	18, 54

*A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <http://www.aafp.org/afpsort.xml>.*

**Table 1. Diagnostic Findings and Appropriate Treatments for Upper Respiratory Tract Infections**

Condition	Key diagnostic findings	Treatment
Acute bronchitis and tracheitis	Cough, possible phlegm production	Symptomatic treatment; antibiotics are not recommended <sup>3-6</sup>
Acute otitis media	Acute onset of symptoms, presence of middle ear effusion, signs of middle ear inflammation	Amoxicillin, 80 to 90 mg per kg per day, in two divided doses (first-line treatment) <sup>7-9</sup>
Acute rhinosinusitis	Nasal obstruction, anterior or posterior purulent nasal discharge, facial pain, cough, decreased sense of smell	Watchful waiting in mild cases; amoxicillin for severe or complicated bacterial rhinosinusitis <sup>10</sup>
Common cold	Runny nose, cough, sore throat, sneezing, nasal congestion	Symptomatic treatment; antibiotics are not recommended <sup>11</sup>
Epiglottitis	Dysphagia, voice change, tachycardia (heart rate > 100 beats per minute), drooling, fever, subjective shortness of breath, tachypnea (respiratory rate > 24 breaths per minute), stridor, respiratory distress, leaning forward	Intravenous combination of a third-generation cephalosporin and an antistaphylococcal agent active against methicillin-resistant <i>Staphylococcus aureus</i> <sup>12</sup> or intravenous monotherapy with ceftriaxone (Rocephin), cefotaxime (Claforan), or ampicillin/sulbactam (Unasyn) <sup>13-15</sup>
Influenza	Abrupt onset of fever, headache, myalgia, malaise	Influenza vaccination for prevention; supportive care; initiation of antiviral therapy within 48 hours of symptom onset may decrease illness duration by one day <sup>16,17</sup>
Laryngitis	Loss or muffling of voice, sore throat, cough, fever, runny nose, headache	Symptomatic treatment; antibiotics are unnecessary <sup>18</sup>
Pharyngitis and tonsillitis	Sore throat, fever, absence of cough	Treatment based on modified Centor score (Table 2)

*Information from references 3 through 18.*

Patients with severe illness, those older than 65 years or younger than two years, pregnant women, and those with chronic illnesses should be treated with antivirals.<sup>24</sup> Empiric antibiotic therapy should not be continued after influenza is diagnosed unless there is concern about a secondary bacterial process. Gram stain and cultures of body fluids can be useful in determining whether antibiotics should be added to an antiviral regimen.

### Rhinosinusitis

Acute rhinosinusitis is a common diagnosis in the outpatient setting, with an annual incidence of approximately 13 percent in adults.<sup>25</sup> It is defined as inflammation of the nasal mucosa and sinuses. Symptoms include nasal obstruction, anterior or posterior purulent nasal discharge, facial pain, decrease in sense of smell, and cough.<sup>26</sup> Rhinosinusitis is classified as acute when symptoms

are present for less than four weeks, subacute for four to 12 weeks, and chronic for more than 12 weeks.<sup>26</sup>

Differentiating between viral and bacterial rhinosinusitis is important because treatment of all cases would result in the overprescribing of antibiotics.<sup>26</sup> The diagnosis of acute bacterial rhinosinusitis should not be made until symptoms have persisted for at least 10 days or after initial improvement followed by worsening of symptoms.<sup>10</sup> Four symptoms are more predictive of bacterial rather than viral rhinosinusitis: purulent nasal discharge, maxillary tooth or facial pain, unilateral maxillary sinus tenderness, and worsening symptoms after initial improvement.<sup>27,28</sup>

Mild cases of acute bacterial rhinosinusitis can be managed with watchful waiting if appropriate follow-up can be ensured.<sup>10</sup> Worsening symptoms within seven days warrant the initiation of antibiotics in these patients. Antibiotic treatment is acceptable in patients with severe or complicated acute bacterial rhinosinusitis.<sup>28</sup> A Cochrane review of five studies in the primary care setting (n = 631 patients) found that antibiotic therapy for acute maxillary sinusitis has a slight statistical advantage over placebo.<sup>29</sup> However, the clinical significance was equivocal because the clinical cure rate was high in both groups (90 percent in the treatment group compared with 80 percent in the placebo group). The antibiotic chosen should provide coverage for *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*,<sup>30</sup> with amoxicillin as the first choice or trimethoprim/sulfamethoxazole (Bactrim, Septra) for patients allergic to penicillin.<sup>10</sup> A different antibiotic is justified if symptoms worsen within seven days.<sup>10</sup> A meta-analysis of 12 RCTs (10 double-blinded, n = 4,430 patients) found no statistically significant difference between long- and short-course antibiotics for cure or improvement of symptoms.<sup>31</sup> Short-course antibiotic therapy (median of five days' duration) was as effective as longer-course treatment (median of 10 days' duration) in patients with acute, uncomplicated bacterial rhinosinusitis.

### Otitis Media

The diagnosis of acute otitis media (AOM) requires an acute onset of symptoms, the presence of middle ear effusion, and signs and symptoms of middle ear inflammation.<sup>7</sup> The most common pathogens are nontypeable *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis*.<sup>32</sup> Viruses have been found in the respiratory secretions of patients with AOM and may account for many cases of antibiotic failure.<sup>33-35</sup> Group B streptococcus, gram-negative enteric bacteria, and *Chlamydia trachomatis*

are common middle ear pathogens in infants up to eight weeks of age.<sup>8</sup>

Cohort studies and RCTs have shown that AOM typically resolves without antibiotic therapy in children.<sup>36</sup> In 2004, the American Academy of Pediatrics and the American Academy of Family Physicians developed guidelines for the treatment of AOM.<sup>7</sup> These guidelines list observation as an option for children older than six months; observation involves deferring antibiotic treatment for 48 to 72 hours and initiating therapy only if symptoms persist or worsen. However, two RCTs conducted in 2011 found that immediate antibiotic use in children six to 35 months of age was more effective than observation.<sup>37,38</sup> These studies used strict criteria, tympanometry, or otoscopy for diagnosis and follow-up. Febrile infants (up to eight weeks of age) with AOM should have a full sepsis workup. These infants should undergo an otolaryngology consultation, if available, for tympanocentesis.<sup>8</sup> Immediate initiation of antibiotics is recommended in children younger than two years with bilateral AOM and in those with AOM and otorrhea.<sup>39,40</sup> Amoxicillin (80 to 90 mg per kg per day, in two divided doses) is recommended as first-line treatment for AOM.<sup>7-9</sup>

**Amoxicillin is the first-line antibiotic for treatment of acute otitis media.**

If there is no response to initial antibiotic therapy within 48 to 72 hours, the patient should be reexamined to confirm the diagnosis, and amoxicillin/clavulanate (Augmentin) should be initiated.<sup>7,8</sup> Ceftriaxone (Rocephin) can be used as a second-line agent or in children with vomiting.<sup>7</sup> Trimethoprim/sulfamethoxazole and erythromycin/sulfisoxazole are not effective for the treatment of AOM.<sup>7,8</sup> Longer courses of antibiotics (more than seven days) have lower failure rates than shorter courses.<sup>41</sup>

Children with AOM should be reevaluated in three months to document clearance of middle ear effusion.<sup>8</sup> Long-term antibiotic therapy has been shown to reduce the number of recurrent AOM episodes,<sup>42</sup> but is not recommended because of the risk of antibiotic resistance.<sup>8</sup> Antibiotics are not recommended for the treatment of otitis media with effusion because they have only a modest short-term benefit.<sup>43</sup>

### Pharyngitis and Tonsillitis

Approximately 90 percent of adults and 70 percent of children with pharyngitis have viral infections.<sup>44-46</sup> In those with bacterial cases of pharyngitis, the leading

## Upper Respiratory Tract Infections

pathogen is group A beta-hemolytic streptococcus. Appropriate antibiotic treatment in these cases has been shown to decrease the risk of rheumatic fever, alleviate symptoms, and decrease communicability.<sup>20,45,47</sup> Antibiotic treatment does not prevent glomerulonephritis and has inconsistent results in the prevention of peritonsillar abscess.<sup>20,44</sup>

The Infectious Diseases Society of America recommends diagnostic testing to confirm group A beta-hemolytic streptococcal infection before initiating antibiotics to avoid overuse.<sup>45</sup> However, the American Academy of Family Physicians and the American College of Physicians recommend using the modified Centor criteria, which are based on age and the presence or absence of fever, tonsillar erythema or exudates, anterior cervical lymphadenopathy, and cough<sup>48-51</sup> (Table 2<sup>47-50</sup>). In patients with a score of 1 or less, no further diagnostic testing or treatment is indicated because the likelihood of streptococcal infection is low. However, in patients

**Approximately 90 percent of adults and 70 percent of children with pharyngitis have viral infections.**

with a score of 1, other factors should be considered, such as contact with a person who has documented streptococcal infection;

rapid antigen detection testing should be performed in these patients. In those with a score of 2 or 3, streptococcal rapid antigen detection testing should also be performed. If test results are positive, antibiotic treatment is indicated. Antibiotic therapy is recommended for patients with a score of 4 or 5.<sup>49</sup>

The recommended first-line treatment is a 10-day course of penicillin.<sup>45,49,52</sup> Erythromycin can be used in patients who are allergic to penicillin.<sup>49,53</sup> Amoxicillin, azithromycin (Zithromax), and first-generation cephalosporins are appropriate alternatives.<sup>45,49</sup>

### Laryngitis

Acute laryngitis is inflammation of the vocal cords and larynx lasting less than three weeks.<sup>54</sup> Symptoms include loss or muffling of the voice, sore throat, and other classic URI symptoms such as cough, fever, runny nose, and headache. A Cochrane review of antibiotic therapy in patients with laryngitis found two studies (n = 206 patients) showing that antibiotic use does not reduce the duration of symptoms or lead to voice improvement.<sup>54</sup> Although these studies are older, there are no recent studies to indicate that these conclusions have changed. Laryngitis is a self-limited, viral disease that does not respond to antibiotic therapy.<sup>18</sup>

### Epiglottitis

Epiglottitis is an inflammatory condition of the epiglottis and adjacent supraglottic structures that can rapidly progress to airway compromise and, potentially, death.<sup>55,56</sup> The incidence of epiglottitis in children has decreased with the use of *H. influenzae* type b (Hib) conjugate vaccines in early infancy.<sup>13,57</sup> A combination of an intravenous antistaphylococcal agent that is active against methicillin-resistant *Staphylococcus aureus* and a third-generation cephalosporin may be effective.<sup>12</sup> Intravenous monotherapy with ceftriaxone, cefotaxime (Claforan), or ampicillin/sulbactam (Unasyn) is also recommended.<sup>13-15</sup>

### Bronchitis and Tracheitis

Acute bronchitis is a self-limited inflammation of the large airways (including the trachea) that presents with cough and possibly phlegm production. The predominant etiology of acute bronchitis is viral; therefore, antibiotics are not indicated in most patients.<sup>3-5,58</sup> Many studies have evaluated the use of antibiotics in the treatment of acute bronchitis and found no significant benefit from their use. Guidelines from the National Institute for Health and Clinical Excellence and the Centers for Disease Control and Prevention do not recommend antibiotics for the treatment of adults with acute bronchitis.<sup>4,5</sup> A 2004 Cochrane review found a small decrease in cough and days of feeling ill in patients who received antibiotics;

**Table 2. Modified Centor Criteria for Pharyngitis and Tonsillitis**

Clinical finding	Points
Absence of cough	1
Age	
3 to 14 years	1
15 to 45 years	0
Older than 45 years	-1
Anterior cervical lymphadenopathy	1
Fever	1
Tonsillar erythema or exudates	1

NOTE: Patients with a score of 1 or less do not require further testing or treatment, although contact with a person who has documented streptococcal infection should be considered in patients with a score of 1, and testing should be performed in these cases; those with a score of 2 or 3 should have rapid antigen detection testing and, if results are positive, should receive antibiotics; and those with a score of 4 or 5 should receive antibiotics.

Information from references 47 through 50.

however, the authors do not recommend their use because of adverse reactions, antibiotic resistance, and cost.<sup>3</sup> Individualized care focusing on symptom relief, as well as explaining to patients why antibiotics are not indicated, is appropriate in managing acute bronchitis in the outpatient setting.

It is important to differentiate pneumonia and influenza from bronchitis because antibiotics are recommended for patients with pneumonia, and antivirals may be indicated for those with influenza. Few cases of acute bronchitis are caused by *Bordetella pertussis* or atypical bacteria, such as *Chlamydia pneumoniae* and *Mycoplasma pneumoniae*. However, these infections are self-limited and do not warrant antibiotic use except in rare cases in which pneumonia develops or the patient is immunocompromised.<sup>5</sup> The British Thoracic Society does not recommend using antibiotics to treat cough or head colds in children except when pertussis is suspected, and then macrolides should be administered early in the course of the disease.<sup>6</sup> In patients with suspected pertussis, antibiotics are prescribed to curb the spread of disease rather than to change patient outcomes.<sup>4</sup>

**Data Sources:** A PubMed search was completed in Clinical Queries using the key terms upper respiratory tract infections, URI, antibiotics, and treatment. The search included meta-analyses, randomized controlled trials, clinical trials, and reviews. Also searched were the Agency for Healthcare Research and Quality evidence reports, Clinical Evidence, the Cochrane database, Essential Evidence Plus, the National Guideline Clearinghouse database, and DynaMed. Search date: September 29, 2011.

## The Authors

ROGER ZOOROB, MD, MPH, is a Frank S. Royal Sr. Professor and Chair of the Department of Family and Community Medicine at Meharry Medical College in Nashville, Tenn., and a professor and director of family medicine at Vanderbilt University in Nashville.

MOHAMAD A. SIDANI, MD, MS, is a professor and vice chair for clinical affairs in the Department of Family and Community Medicine at Meharry Medical College.

RICHARD D. FREMONT, MD, is an assistant professor of medicine and chief of pulmonary and critical care medicine at Meharry Medical College.

COURTNEY KIHLEBERG, MD, MSPH, is an assistant professor of family and community medicine at Meharry Medical College.

*Address correspondence to Roger Zoorob, MD, MPH, Meharry Medical College, 1005 Dr. D.B. Todd Blvd., Nashville, TN 37208 (e-mail: rzoorob@mmc.edu). Reprints are not available from the authors.*

Author disclosure: No relevant financial affiliations to disclose.

## REFERENCES

- Heikkinen T, Järvinen A. The common cold. *Lancet*. 2003;361(9351):51-59.
- Gonzales R, Malone DC, Maselli JH, Sande MA. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis*. 2001;33(6):757-762.
- Smucny J, Fahey T, Becker L, Glazier R. Antibiotics for acute bronchitis. *Cochrane Database Syst Rev*. 2004;(4):CD000245.
- Gonzales R, Bartlett JG, Besser RE, et al.; American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine; Centers for Disease Control; Infectious Diseases Society of America. Principles of appropriate antibiotic use for treatment of uncomplicated acute bronchitis: background. *Ann Intern Med*. 2001;134(6):521-529.
- National Institute for Health and Clinical Excellence. Respiratory tract infections—antibiotic prescribing. <http://www.nice.org.uk/nicemedia/live/12015/41323/41323.pdf>. Accessed August 14, 2012.
- Shields MD, Bush A, Everard ML, McKenzie S, Primhak R; British Thoracic Society Cough Guideline Group. BTS guidelines: recommendations for the assessment and management of cough in children. *Thorax*. 2008;63(suppl 3):iii1-iii15.
- American Academy of Pediatrics Subcommittee on Management of Acute Otitis Media. Diagnosis and management of acute otitis media. *Pediatrics*. 2004;113(5):1451-1465.
- University of Michigan Health System. Guidelines for clinical care: otitis media. <http://www.med.umich.edu/inf/fhp/practiceguides/om/OM.pdf>. Accessed August 14, 2012.
- Coker TR, Chan LS, Newberry SJ, et al. Diagnosis, microbial epidemiology, and antibiotic treatment of acute otitis media in children: a systematic review. *JAMA*. 2010;304(19):2161-2169.
- Rosenfeld RM, Andes D, Bhattacharyya N, et al. Clinical practice guideline: adult sinusitis. *Otolaryngol Head Neck Surg*. 2007;137(3 suppl):S1-S31.
- Arroll B, Kenealy T. Antibiotics for the common cold and acute purulent rhinitis. *Cochrane Database Syst Rev*. 2005;(3):CD000247.
- Ward MA. Emergency department management of acute respiratory infections. *Semin Respir Infect*. 2002;17(1):65-71.
- Shah RK, Roberson DW, Jones DT. Epiglottitis in the *Haemophilus influenzae* type b vaccine era: changing trends. *Laryngoscope*. 2004;114(3):557-560.
- Tanner K, Fitzsimmons G, Carrol ED, Flood TJ, Clark JE. *Haemophilus influenzae* type b epiglottitis as a cause of acute upper airways obstruction in children. *BMJ*. 2002;325(7372):1099-1100.
- Fairbanks DN. Pocket guide to antimicrobial therapy in otolaryngology—head and neck surgery. 13 ed. <http://www.entnet.org/EducationAndResearch/upload/AAO-PGS-9-4-2.pdf>. Accessed August 14, 2012.
- Treanor JJ, Hayden FG, Vrooman PS, et al.; US Oral Neuraminidase Study Group. Efficacy and safety of the oral neuraminidase inhibitor oseltamivir in treating acute influenza: a randomized controlled trial. *JAMA*. 2000;283(8):1016-1024.
- Jefferson T, Demicheli V, Rivetti D, Jones M, Di Pietrantonj C, Rivetti A. Antivirals for influenza in healthy adults: systematic review [published correction appears in *Lancet*. 2006;367(9528):2060]. *Lancet*. 2006;367(9507):303-313.
- Schwartz SR, Cohen SM, Dailey SH, et al. Clinical practice guideline: hoarseness (dysphonia). *Otolaryngol Head Neck Surg*. 2009;141(3 suppl 2):S1-S31.
- Gill JM, Fleischut P, Haas S, Pellini B, Crawford A, Nash DB. Use of antibiotics for adult upper respiratory infections in outpatient settings: a national ambulatory network study. *Fam Med*. 2006;38(5):349-354.
- Centor RM, Allison JJ, Cohen SJ. Pharyngitis management: defining the controversy. *J Gen Intern Med*. 2007;22(1):127-130.
- Winther B. Rhinovirus infections in the upper airway. *Proc Am Thorac Soc*. 2011;8(1):79-89.
- Steinman MA, Gonzales R, Linder JA, Landefeld CS. Changing use of antibiotics in community-based outpatient practice, 1991-1999. *Ann Intern Med*. 2003;138(7):525-533.
- Harper SA, Bradley JS, Englund JA, et al.; Expert Panel of the Infectious Diseases Society of America. Seasonal influenza in adults and children—diagnosis, treatment, chemoprophylaxis, and institutional

- outbreak management: clinical practice guidelines of the Infectious Diseases Society of America. *Clin Infect Dis*. 2009;48(8):1003-1032.
24. Fiore AE, Fry A, Shay D, Gubareva L, Bresee JS, Uyeki TM; Centers for Disease Control and Prevention (CDC). Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep*. 2011;60(1):1-24.
  25. Centers for Disease Control and Prevention. Summary health statistics for U.S. adults: National Health Interview Survey, 2009. [http://www.cdc.gov/nchs/data/series/sr\\_10/sr10\\_249.pdf](http://www.cdc.gov/nchs/data/series/sr_10/sr10_249.pdf). Accessed August 14, 2012.
  26. Thomas M, Yawn BP, Price D, Lund V, Mullol J, Fokkens W; European Position Paper on Rhinosinusitis and Nasal Polyps Group. EPOS primary care guidelines: European position paper on the primary care diagnosis and management of rhinosinusitis and nasal polyps 2007—a summary. *Prim Care Respir J*. 2008;17(2):79-89.
  27. Gonzales R, Bartlett JG, Besser RE, Hickner JM, Hoffman JR, Sande MA; American Academy of Family Physicians; Infectious Diseases Society of America; Centers for Disease Control; American College of Physicians-American Society of Internal Medicine. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults: background. *Ann Intern Med*. 2001;134(6):490-494.
  28. Chow AW, Benninger MS, Brook I, et al.; Infectious Diseases Society of America. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis*. 2012;54(8):e72-e112.
  29. Williams JW Jr, Aguilar C, Cornell J, et al. Antibiotics for acute maxillary sinusitis. *Cochrane Database Syst Rev*. 2008;(2):CD000243.
  30. Poole MD. Acute bacterial rhinosinusitis: clinical impact of resistance and susceptibility. *Am J Med*. 2004;117(suppl 3A):29S-38S.
  31. Falagas ME, Karageorgopoulos DE, Grammatikos AP, Matthaïou DK. Effectiveness and safety of short vs. long duration of antibiotic therapy for acute bacterial sinusitis: a meta-analysis of randomized trials. *Br J Clin Pharmacol*. 2009;67(2):161-171.
  32. Klein JO. Otitis media. *Clin Infect Dis*. 1994;19(5):823-833.
  33. Heikkinen T, Thint M, Chonmaitree T. Prevalence of various respiratory viruses in the middle ear during acute otitis media. *N Engl J Med*. 1999;340(4):260-264.
  34. Pitkäranta A, Virolainen A, Jero J, Arruda E, Hayden FG. Detection of rhinovirus, respiratory syncytial virus, and coronavirus infections in acute otitis media by reverse transcriptase polymerase chain reaction. *Pediatrics*. 1998;102(2 pt 1):291-295.
  35. Chonmaitree T. Viral and bacterial interaction in acute otitis media. *Pediatr Infect Dis J*. 2000;19(5 suppl):S24-S30.
  36. Rosenfeld RM, Kay D. Natural history of untreated otitis media. *Laryngoscope*. 2003;113(10):1645-1657.
  37. Tähtinen PA, Laine MK, Huovinen P, Jalava J, Ruuskanen O, Ruohola A. A placebo-controlled trial of antimicrobial treatment for acute otitis media. *N Engl J Med*. 2011;364(2):116-126.
  38. Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. *N Engl J Med*. 2011;364(2):105-115.
  39. Rovers MM, Glasziou P, Appelman CL, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet*. 2006;368(9545):1429-1435.
  40. Glasziou PP, Del Mar CB, Sanders SL, Hayem M. Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev*. 2004;(1):CD000219.
  41. Kozyrskyj A, Klassen TP, Moffatt M, Harvey K. Short-course antibiotics for acute otitis media. *Cochrane Database Syst Rev*. 2010;(9):CD001095.
  42. Leach AJ, Morris PS. Antibiotics for the prevention of acute and chronic suppurative otitis media in children. *Cochrane Database Syst Rev*. 2006;(4):CD004401.
  43. American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Otitis media with effusion. *Pediatrics*. 2004;113(5):1412-1429.
  44. Institute for Clinical Systems Improvement. Diagnosis and treatment of respiratory illness in children and adults: percentage of patients with strep pharyngitis who had rapid group A strep test or strep culture. <http://qualitymeasures.ahrq.gov/content.aspx?id=32415>. Accessed September 26, 2012.
  45. Bisno AL, Gerber MA, Gwaltney JM Jr, Kaplan EL, Schwartz RH; Infectious Diseases Society of America. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis. *Clin Infect Dis*. 2002;35(2):113-125.
  46. Bisno AL. Acute pharyngitis: etiology and diagnosis. *Pediatrics*. 1996;97(6 pt 2):949-954.
  47. Cooper RJ, Hoffman JR, Bartlett JG, et al.; American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine; Centers for Disease Control. Principles of appropriate antibiotic use for acute pharyngitis in adults: background. *Ann Intern Med*. 2001;134(6):509-517.
  48. Ebell MH. Making decisions at the point of care: sore throat. *Fam Pract Manag*. 2003;10(8):68-69.
  49. Choby BA. Diagnosis and treatment of streptococcal pharyngitis. *Am Fam Physician*. 2009;79(5):383-390.
  50. McIsaac WJ, White D, Tannenbaum D, Low DE. A clinical score to reduce unnecessary antibiotic use in patients with sore throat. *CMAJ*. 1998;158(1):75-83.
  51. McIsaac WJ, Goel V, To T, Low DE. The validity of a sore throat score in family practice. *CMAJ*. 2000;163(7):811-815.
  52. Lan AJ, Colford JM, Colford JM Jr. The impact of dosing frequency on the efficacy of 10-day penicillin or amoxicillin therapy for streptococcal tonsillopharyngitis: a meta-analysis. *Pediatrics*. 2000;105(2):E19.
  53. Snow V, Mottur-Pilson C, Cooper RJ, Hoffman JR; American Academy of Family Physicians; American College of Physicians-American Society of Internal Medicine; Centers for Disease Control. Principles of appropriate antibiotic use for acute pharyngitis in adults. *Ann Intern Med*. 2001;134(6):506-508.
  54. Reveiz L, Cardona AF, Ospina EG. Antibiotics for acute laryngitis in adults. *Cochrane Database Syst Rev*. 2007;(2):CD004783.
  55. Rafei K, Lichenstein R. Airway infectious disease emergencies. *Pediatr Clin North Am*. 2006;53(2):215-242.
  56. Guldred LA, Lyhne D, Becker BC. Acute epiglottitis: epidemiology, clinical presentation, management and outcome. *J Laryngol Otol*. 2008;122(8):818-823.
  57. González Valdepeña H, Wald ER, Rose E, Ungkanont K, Casselbrant ML. Epiglottitis and *Haemophilus influenzae* immunization: the Pittsburgh experience—a five-year review. *Pediatrics*. 1995;96(3 pt 1):424-427.
  58. Irwin RS, Baumann MH, Bolser DC, et al.; American College of Chest Physicians (ACCP). Diagnosis and management of cough executive summary: ACCP evidence-based clinical practice guidelines. *Chest*. 2006;129(1 suppl):1S-23S.