

Principles of Appropriate Antibiotic Use for Acute Rhinosinusitis in Adults: Background

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The following principles of appropriate antibiotic use for adults with acute rhinosinusitis apply to the diagnosis and treatment of acute maxillary and ethmoid rhinosinusitis in adults who are not immunocompromised.

1. Most cases of acute rhinosinusitis diagnosed in ambulatory care are caused by uncomplicated viral upper respiratory tract infections.

2. Bacterial and viral rhinosinusitis are difficult to differentiate on clinical grounds. The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for patients with rhinosinusitis symptoms lasting 7 days or more who have maxillary pain or tenderness in the face or teeth (especially when unilateral) and purulent nasal secretions. Patients with rhinosinusitis symptoms that last less than 7 days are unlikely to have bacterial infection, although rarely some patients with acute bacterial rhinosinusitis present with dramatic symptoms of severe unilateral maxillary pain, swelling, and fever.

3. Sinus radiography is not recommended for diagnosis in routine cases.

4. Acute rhinosinusitis resolves without antibiotic treatment in most cases. Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms. Antibiotic therapy should be reserved for patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis and for those with severe rhinosinusitis symptoms—especially those with unilateral facial pain—regardless of duration of illness. For initial treatment, the most narrow-spectrum agent active against the likely pathogens, *Streptococcus pneumoniae* and *Haemophilus influenzae*, should be used.

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1.0 The excessive use of antibiotics in ambulatory practice has contributed to the emergence and spread of antibiotic-resistant bacteria.¹⁻⁴ Antibiotic treatment of common respiratory infections accounts for a large percentage of this excessive use. Rhinosinusitis is one of the 10 most common diagnoses in ambulatory practice and is the cause of an estimated 25 million U.S. physician office visits in 1995.⁵ Fourteen percent of Americans claim to have had a previous diagnosis of sinusitis,⁶ but the term *sinusitis* typically has a different meaning for patients and for primary care physicians. When patients say “I have sinus trouble,” they usually describe acute or chronic symptoms, such as headache, facial pain, nasal congestion, or rhinorrhea, each of which may be due to a variety of causes. Primary care physicians tend to think of sinusitis as an acute bacterial infection, for which they prescribe an antibiotic in 85% to 98% of cases.^{7,8} According to data from the National Ambulatory Medical Care Survey, sinusitis is the fifth most common diagnosis for which an antibiotic is prescribed.⁹ However, sinusitis is frequently caused by viral infection and will resolve in most patients without antibiotic treatment. These principles present an argument for a conservative approach to use of antibiotics in patients with sinusitis-like symptoms, consistent with efforts to reduce antibiotic use for respiratory infections in ambulatory patients. Background, rationale, and methods used for development of these principles have been published separately.¹⁰

1.1 The term *sinusitis* refers to inflammation of the mucosa of the paranasal sinuses, regardless of cause. Because sinusitis is invariably accompanied by inflammation of the contiguous nasal mucosa, *rhinosinusitis* has become the preferred term. Most cases of rhinosinusitis involve more than one of the paranasal sinuses, most commonly the maxillary and ethmoid sinuses. Isolated infection of a frontal or sphenoid sinus is a rare and potentially dangerous condition, usually caused by bacteria, which presents very differently from the vast majority of cases of rhinosinusitis seen in primary care. Patients with this type of infection seem seriously ill and may show signs of cavernous sinus thrombosis or meningitis. Diagnosis and treatment of isolated frontal and sphenoid sinusitis are beyond the scope of this discussion.

For purposes of diagnosis and treatment, rhinosinusitis is classified as acute (symptom duration <4 weeks), subacute (symptom duration 4 to 12 weeks), and chronic (symptom duration >12 weeks).¹¹ Patients may have recurrent acute attacks or acute exacerbations of chronic rhinosinusitis. Chronic and subacute bacterial sinus infections may require surgical consultation and manage-

ment. Acute rhinosinusitis, however, makes up most cases in ambulatory care, and primary care clinicians treat most of these infections without consultation. These principles are limited to the diagnosis and treatment of acute maxillary and ethmoid rhinosinusitis in immunocompetent adults.

1.2 Acute bacterial rhinosinusitis is usually a secondary infection resulting from sinus ostia obstruction or impairment of mucus clearance mechanisms caused by an acute viral upper respiratory tract infection.¹² *Streptococcus pneumoniae* and *Haemophilus influenzae* are the bacteria most commonly isolated from infected maxillary sinuses.¹³ *Streptococcus pyogenes*, *Moraxella catarrhalis*, and anaerobic bacteria each account for a small percentage of bacterial sinus infections. Current reviews providing more details of the pathogenesis of acute and chronic sinusitis have recently been published.^{11,13} The gold standard for diagnosis of bacterial rhinosinusitis is sinus puncture with aspiration of purulent secretions that yield growth on culture of at least 10⁵ organisms per milliliter of a likely respiratory pathogen.¹⁴ However, sinus puncture is an invasive procedure seldom performed in primary care and is usually indicated only in complicated cases, such as those resistant to treatment. Because no simple and accurate office-based tests for acute bacterial rhinosinusitis are available, clinicians rely on clinical findings to make the diagnosis. However, signs and symptoms of acute bacterial rhinosinusitis and of prolonged viral upper respiratory tract infections are extraordinarily similar, making the clinical diagnosis of acute bacterial rhinosinusitis difficult and resulting in frequent misclassification of viral cases.

Antibiotics have potential value in treating acute rhinosinusitis only when true bacterial infection is present. Therefore, two issues must be addressed before use of antibiotics is considered for acute rhinosinusitis. First, can one reliably differentiate acute bacterial rhinosinusitis from acute viral rhinosinusitis and, if so, how? Second, are antibiotics effective in treatment of acute bacterial rhinosinusitis and, if so, how effective?

PRINCIPLES

Principle 1. Most cases of acute rhinosinusitis diagnosed in ambulatory care are caused by uncomplicated viral upper respiratory tract infections [A]. (Letters in square brackets are evidence ratings. See the background document in this issue¹⁰ for explanation.)

2.0 Causes of acute sinus inflammation include infection, allergy, and local irritants. Cases due to allergy and

irritants can usually be distinguished from infection on the basis of a careful history. Symptoms due to allergy and environmental irritants are usually more chronic or recurrent, are infrequently associated with purulent nasal discharge, frequently include itching and sneezing, and are often associated with specific exposures. Adult patients are often accurate in self-diagnosis of allergic rhinitis.¹⁵ Infectious causes of acute rhinosinusitis include respiratory viruses, fungi, and bacteria. Fungal infections are rare in immunocompetent hosts. Viruses cause most cases of acute sinus inflammation. Maxillary sinus radiographs of young adults with typical viral upper respiratory tract infections showed mucosal abnormalities in 39% of cases on the seventh day of illness,¹⁶ and computed tomographic scans were abnormal in 87% of similar cases.¹⁷ These studies show that some degree of sinus mucosa inflammation is very common in viral upper respiratory tract infections. On the basis of epidemiologic estimates, only 0.2% to 2% of viral upper respiratory tract infections in adults are complicated by bacterial rhinosinusitis,^{18,19} and approximately 15% of people with symptoms of acute respiratory infection seek medical care.²⁰ Presuming a 2% bacterial rhinosinusitis infection rate, if all patients with bacterial rhinosinusitis were among those seeking care, no more than approximately 13% (0.02/0.15) of patients who presented with symptoms of acute respiratory infection would have bacterial rhinosinusitis. Yet the ratio of cases in which primary care physicians diagnose upper respiratory tract infection and acute rhinosinusitis in adults is approximately 1:1,^{7,8} suggesting that clinicians frequently misclassify viral upper respiratory tract infections as acute bacterial rhinosinusitis.

Principle 2. Bacterial and viral rhinosinusitis are difficult to differentiate on clinical grounds [B].

The clinical diagnosis of acute bacterial rhinosinusitis should be reserved for patients with rhinosinusitis symptoms lasting 7 days or more who have maxillary pain or tenderness in the face or teeth (especially when unilateral) and purulent nasal secretions. Patients who have rhinosinusitis symptoms for less than 7 days are unlikely to have bacterial infection.

3.0 Overdiagnosis of acute bacterial rhinosinusitis is not surprising, considering the lack of specific clinical features that distinguish it from nonbacterial upper respiratory tract infections. Relying on overall clinical impression, primary care physicians classifying patients as highly likely to have bacterial rhinosinusitis are correct in approximately 40% to 50% of cases.¹⁸⁻²² Often, patients and physicians believe that an upper respiratory tract infection “has gone on for too long” and that antibiotic

treatment is therefore needed. Gwaltney and colleagues²¹ studied the natural history of rhinovirus illness in young adults. Length of illness ranged from 1 to 33 days, and only one fourth of the patients had symptoms lasting longer than 14 days. Most were well or nearly well in 7 to 10 days. However, in clinical trials of diagnosis and treatment of rhinosinusitis, duration of illness alone does not reliably distinguish prolonged viral infection from bacterial rhinosinusitis (Williams J, Hansen JG, Lindbaek M. Personal communication). For example, Lindbaek found that, among patients with sinusitis-like symptoms referred from primary care physicians, 80% of those with computed tomography criteria for bacterial sinusitis (air-fluid level or total opacification) had had symptoms for longer than 7 days, while 70% of those without computed tomography criteria for bacterial rhinosinusitis also had symptoms for more than 7 days. Nonetheless, bacterial rhinosinusitis was seen in only 20% of patients whose symptoms lasted less than 7 days (Lindbaek M. Personal communication). Therefore, duration of symptoms of 7 days or greater is a moderately sensitive but nonspecific predictor of bacterial rhinosinusitis.

3.1 Aside from duration of illness, are any symptoms and signs helpful in distinguishing between bacterial and viral rhinosinusitis? Since 1976, seven investigators have published reports attempting to identify signs and symptoms specific to acute bacterial rhinosinusitis.²²⁻²⁸ All seven studies are limited by use of imperfect diagnostic standards. None used the best criterion for diagnosing bacterial rhinosinusitis, which is aspiration of purulent secretions on sinus puncture that grow at least 10^5 organisms per milliliter of a likely respiratory pathogen on culture. The findings of these trials, listed by diagnostic standard, are summarized in the Table. No single sign or symptom had strong diagnostic value in any study, although certain combinations of signs and symptoms seem to be helpful.

3.1.1 The study by Hansen and coworkers²² is the best of the seven. The authors studied 172 patients with suspected bacterial rhinosinusitis referred from general practitioners in Denmark and used maxillary sinus aspiration of purulent or mucopurulent fluid as the diagnostic criterion. Of these patients, 53% had pus or mucopurulent fluid on sinus aspiration, and of this 53%, three fourths had positive bacterial cultures. Unilateral maxillary pain, maxillary toothache, unilateral tenderness of the maxillary sinus, and mucopurulent nasal discharge were statistically more likely in patients with positive sinus aspirates. However, the magnitude of association was small (odds ratio, 1.9 to 2.5), and these findings

were common in patients with and without bacterial infection. The results of the study did not change when analyzed by culture results.

In patients presenting to an emergency department with sinusitis-like symptoms of less than 3 months' duration, Berg and Carenfelt²³ noted that the following four findings were associated with an increased likelihood of bacterial infection (defined as purulent secretions on sinus aspiration): a history of purulent nasal discharge with unilateral predominance, a history of facial pain with unilateral predominance, a history of bilateral purulent nasal discharge, and pus in the nasal cavity on physical examination. When at least two of these findings were present, 67% to 85% of patients had bacterial rhinosinusitis. If one or none were present, fewer than 10% had bacterial infection. The relevance of Berg and Carenfelt's findings to patients with acute rhinosinusitis in primary care is limited by inclusion of patients whose symptoms had lasted for more than 30 days.

3.1.2 The five other investigators²⁴⁻²⁸ used noninvasive sinus imaging for the diagnosis of acute bacterial rhinosinusitis, including plain radiography, computed tomography scanning, and ultrasonography. Lindbaek and associates²⁴ used air-fluid level or complete sinus opacification on computed tomography sinus radiography as the diagnostic standard. In patients with high clinical probability of bacterial rhinosinusitis, these techniques have an approximately 90% positive predictive value for purulent or mucopurulent secretions on sinus aspiration. Lindbaek found that worsening of symptoms of upper

respiratory tract infection after initial improvement, purulent rhinorrhea, and purulent secretions in the nasal cavities were the best independent clinical predictors of acute rhinosinusitis.

3.1.3 Using plain radiography as the diagnostic standard, Williams and colleagues²⁵ identified five independent predictors of acute bacterial rhinosinusitis in a study of men with suspected rhinosinusitis in a Veterans Administration outpatient clinic. The five predictors were history of colored nasal discharge, purulent nasal secretions on examination, poor response to decongestants, maxillary toothache, and abnormal transillumination. Previous upper respiratory tract infection, purulent rhinorrhea, facial pain on bending forward, unilateral maxillary pain, and tooth pain were significantly associated with positive ultrasonography in a Dutch study of 400 primary care patients with 441 episodes of suspected rhinosinusitis.²⁶ Studies that rely on plain sinus radiography or ultrasonography as the diagnostic standard must be interpreted cautiously because these techniques overestimate the presence of bacterial infection by as much as 50%, offering a large opportunity for misclassification bias.^{29,30}

3.2 Considering the results of all seven studies, purulent nasal discharge, maxillary tooth or facial pain (especially when unilateral), unilateral maxillary sinus tenderness, and worsening of symptoms after initial improvement seem to be helpful for predicting a higher likelihood of bacterial infection in patients with rhinosinusitis-like symptoms. Although generalized facial pain or tenderness, postnasal drainage, headache, and cough

Table.
Studies on the clinical diagnosis of acute rhinosinusitis.

| Study (Reference) | Year | Diagnostic Standard | Sample Size (n) | Predictors of Bacterial Rhinosinusitis |
|-------------------------|------|--|-----------------|--|
| Hansen et al (22) | 1995 | Sinus puncture (presence of purulent or mucopurulent material) | 174 | Purulent or mucopurulent nasal discharge, unilateral maxillary pain, maxillary toothache, unilateral maxillary tenderness |
| Berg and Carenfelt (23) | 1988 | Sinus puncture (presence of purulent or mucopurulent material) | 155 | Purulent rhinorrhea, unilateral facial pain, pus in the nasal cavity |
| Lindbaek et al (24) | 1996 | Computed tomography (air-fluid level or complete opacity) | 127 | Purulent rhinorrhea, purulent secretions, "double sickening"* |
| Williams et al (25) | 1992 | Abnormal results on sinus radiography (mucosal thickening >6 mm, air-fluid level, or complete opacity) | 247 | Maxillary toothache, poor response to decongestants or antihistamines, history of colored nasal discharge, mucopurulent nasal discharge on examination |
| Axelsson and Runze (28) | 1976 | Abnormal results on sinus radiography (mucosal thickening >6 mm or complete opacity) | 164 | Purulent rhinorrhea, previous upper respiratory tract infection, cough, hyposmia, malaise |
| van Duijn et al (26) | 1992 | Abnormal results on ultrasonography | 212 | Previous common cold, purulent rhinorrhea, facial pain on bending forward, unilateral maxillary pain, maxillary tooth pain |
| van Buchem et al (27) | 1995 | Sinus radiography, sonography, or sinus puncture | 113 | No consistent predictors |

*Worsening of symptoms after initial improvement.

are commonly thought to have diagnostic value, no convincing evidence shows that they are helpful in distinguishing acute bacterial rhinosinusitis from prolonged viral rhinosinusitis. A previous diagnosis of rhinosinusitis is also not a predictor of bacterial rhinosinusitis.

Principle 3. Sinus radiography is not recommended for diagnosis in routine cases [B].

4.0 Several investigators have studied the accuracy of sinus radiography in predicting the presence of purulent sinus fluid by using complete opacification, air-fluid level, or various degrees of mucosa thickening as the diagnostic criteria.³¹⁻³⁴ Complete opacification and air-fluid level are the most specific findings, with specificities of 85% (range, 76% to 91%) and 80% (range, 71% to 87%), respectively.³⁰ The finding of mucosal thickening has a low specificity, probably no better than that of skilled clinical judgment, which is 40% to 50%. The absence of all three findings has an estimated sensitivity of approximately 90% and is helpful in ruling out bacterial rhinosinusitis.³⁵ Given these test characteristics and the known high prevalence of abnormal radiography findings in patients with viral rhinosinusitis, sinus radiography has limited value in routine diagnosis of acute bacterial rhinosinusitis.

Principle 4. Acute rhinosinusitis resolves without antibiotic treatment in most cases [A].

Symptomatic treatment and reassurance is the preferred initial management strategy for patients with mild symptoms. Antibiotic therapy should be reserved for patients with moderately severe symptoms who meet the criteria for the clinical diagnosis of acute bacterial rhinosinusitis (symptoms that last >7 days and include maxillary pain in the face or teeth and purulent nasal secretions) and for those with severe rhinosinusitis symptoms, regardless of duration of illness. For initial treatment, the most narrow-spectrum agent that is active against the likely pathogens, *S. pneumoniae* and *H. influenzae*, should be used.

5.0 Randomized, double-blind, placebo-controlled trials of antibiotic treatment for acute bacterial rhinosinusitis using pretreatment and post-treatment culture of sinus aspirates have not been performed. However, non-randomized treatment trials have shown appropriate antibiotics to be highly effective in eradicating or substantially reducing bacterial growth in the sinuses.¹³ Antibiotic treatment is effective from a bacteriologic standpoint. Is it effective from a clinical standpoint?

5.1 Five randomized, double-blind clinical trials with good methods have compared antibiotics with placebo for treatment of acute rhinosinusitis in adults.³⁵⁻³⁹ Two meta-analyses, one performed under the auspices of the Cochrane Collaboration⁴⁰ and the other performed under

contract from the Agency for Healthcare Research and Quality,⁴¹ have recently been published. Both studies concluded that, although antibiotics are statistically more effective than placebo in reducing or eliminating symptoms at 10 and 14 days, the effect size (degree of benefit) is relatively small and most placebo-treated patients improve without antibiotic therapy.

The specific findings of each of these five trials are well summarized by Williams and coworkers.⁴⁰ Four used plain radiography for diagnosis of sinusitis,³⁶⁻³⁹ and one³⁵ used computed tomography. When considered in aggregate, 47% of the antibiotic-treated patients and 32% of controls were considered cured at 10 to 14 days of follow-up, while 81% of antibiotic-treated patients and 66% of controls were responders (with clinical findings of either cure or improvement).³⁹ This is an absolute benefit of 15%, with a number needed to treat for benefit of approximately seven.

5.2 However, the two most recent placebo-controlled trials of acute rhinosinusitis in primary care failed to find a significant clinical effect of antibiotic treatment. Stalman and colleagues³⁸ studied the effectiveness of doxycycline compared with placebo in general practice patients with symptoms of bacterial rhinosinusitis. The inclusion criteria were based on guidelines of the Dutch College of General Practitioners: three main symptoms (reports of symptoms after a common cold or influenza, purulent nasal discharge, and pain in the maxillary sinuses on bending forward) or two main symptoms and one other symptom (predominately unilateral maxillary pain, toothache, or pain when chewing). There was no significant difference in time to resolution of facial pain and return to normal activities. Using radiography as the diagnostic standard, van Buchem and associates⁴⁰ found no statistically significant advantage of a 7-day course of amoxicillin over placebo at follow-up on day 14. Symptoms were substantially improved or resolved in 83% of patients receiving amoxicillin and 77% of patients receiving placebo.

The one modern placebo-controlled trial in a primary care population that showed a positive treatment effect for amoxicillin or penicillin used computed tomographic scanning for diagnosis and study eligibility.³⁵ Only patients with an air-fluid level or complete opacification of a sinus were eligible for inclusion. At day 10 of treatment, 56% of patients who received placebo, 82% of those who received penicillin, and 89% of those who received amoxicillin were substantially better.

5.3 The reason these clinical trials as a whole show antibiotic treatment of sinusitis to be less efficacious than

one might predict from the bacteriologic studies can be explained by the “Pollyanna” phenomenon.⁴² That is, because the clinical and radiologic diagnosis of acute bacterial rhinosinusitis is inaccurate, the measured treatment effect of antibiotics for the entire treatment group is diluted by the cases that do not truly have bacterial infection. Thus, the treatment trial that used a more specific diagnostic standard (positive results on computed tomography scan) showed a significant benefit for antibiotics. In contrast, the trials using the less-specific diagnostic standards—clinical diagnosis³⁸ and radiographic diagnosis³⁹—did not. High rates of recovery and resolution in the placebo groups could also be caused by symptomatic treatments (local nasal decongestants or analgesics) that have a large impact on illness resolution.

When the 40% to 50% prevalence of bacterial rhinosinusitis in patients whose diagnosis is established by signs and symptoms and the modest effectiveness of antibiotic treatment were considered, a cost-effectiveness model sponsored by the Agency for Healthcare Research and Quality favored antibiotic treatment for patients with moderate to severe symptoms and symptomatic treatment for those with mild symptoms (Balk EM, Zucher DR, Engels EA, Wong JB, Williams JW, Lau J. Strategies for diagnosing and treating acute bacterial sinusitis: a cost-effectiveness analysis. Submitted for publication).

5.4 Three recent meta-analyses have concluded that newer and broad-spectrum antibiotics are not significantly more effective than narrow-spectrum agents.^{40,41,43} However, because of the rapid increase in antibiotic resistance of *S. pneumoniae* and *H. influenzae*, physicians must consider current recommendations for treating infection with these organisms when making treatment decisions.

5.5 Serious complications of acute bacterial rhinosinusitis, such as meningitis, brain abscess, and periorbital cellulitis, are rare, and good data on the frequency of these events in treated compared with untreated patients are not available.⁴¹ An estimated 1 of 95,000 hospital discharges in the United States is for brain abscess, and the proportion of these admissions due to acute sinusitis is unknown.⁴¹ No serious complications have been reported in sinusitis treatment trials among patients who received placebo. Nonetheless, some patients with acute bacterial rhinosinusitis may rarely present with dramatic symptoms of severe unilateral maxillary pain, swelling, and fever. These patients must be treated promptly with an appropriate antibiotic and may require surgical referral for sinus drainage. Patients with a clinical diagnosis of acute bacterial sinusitis who do not respond to antibiotic treatment should be referred for further evaluation.

Additional diagnostic procedures to guide therapy at this juncture may include computed tomography to assess anatomic abnormalities or sinus aspiration for culture.

6.0 The results of eight randomized trials of various symptomatic treatments of rhinosinusitis symptoms in adults have been inconclusive.⁴⁴⁻⁵¹ Topically or orally administered α -adrenergic agents, proteolytic enzymes, mucolytic agents, antihistamines, and corticosteroids have been used. Theoretically, agents that encourage drainage of sinus secretions may be of value. Well-designed placebo-controlled trials of these ancillary treatments are needed to determine their effectiveness in treating acute rhinosinusitis. These treatments can be offered to patients with mild symptoms as an alternative to an antibiotic. Pain control is always important because more than 50% of patients with acute bacterial rhinosinusitis report facial pain.²⁴⁻²⁸ Topical and oral decongestants may ameliorate some of the nasal symptoms and promote mucus clearance. All patients should receive a careful explanation of the rationale for management; they should also be educated about signs and symptoms of worsening that should prompt them to contact a physician.

CONCLUSIONS

7.0 The greatest barrier to efficient antibiotic treatment of acute bacterial rhinosinusitis is lack of a simple and accurate diagnostic test. Until a better test is widely available in office practice, the office diagnosis of acute bacterial rhinosinusitis will continue to depend largely on clinical judgment and will remain imprecise. Duration of illness is a useful clinical criterion because acute bacterial sinusitis is not common in patients whose symptoms last less than 7 days. Patients who do not have persistent maxillary facial or tooth pain or tenderness accompanied by purulent nasal drainage are unlikely to have bacterial rhinosinusitis, regardless of duration of illness. We do not recommend routine sinus radiography or limited sinus computed tomography series given the high prevalence of abnormal radiographic findings in patients with viral rhinosinusitis. Recent recommendations from the Sinus and Allergy Foundation also recommend radiography for patients who do not respond within 72 hours after antibiotics are given.⁵²

7.1 Because most patients with a clinical diagnosis of acute rhinosinusitis improve without antibiotic treatment, symptomatic treatment or reassurance is the preferred initial management strategy, except for patients with moderate to severe symptoms. In most cases, only patients with the specific findings of maxillary pain or tenderness in the

face or teeth and persistent purulent nasal discharge who are not improving after 7 days and those with severe rhinosinusitis symptoms, regardless of duration, should be treated with antibiotics. When an antibiotic is prescribed, it should be the most narrow-spectrum agent that is active against the likely pathogens, *S. pneumoniae* and *H. influenzae*. Prescribing physicians should consider factors that predispose patients to antibiotic-resistant bacteria, such as contact with children in daycare centers or recent antibiotic use. Amoxicillin is commonly recommended, and previous reviews have failed to demonstrate that any antibiotic is superior to amoxicillin in clinical response. According to many authorities, amoxicillin continues to be the favored drug, although higher-than-customary doses may be required in some cases.⁵²

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