CLINICAL PRACTICE

Acute Bacterial Sinusitis in Children

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This Journal *feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors' clinical recommendations.*

A 4-year-old girl who attends day care presents with rhinorrhea and a daytime cough that have been present for 12 days. She has not had fever, but her appetite is poor and her interest in activities is diminished. On physical examination, there is clear rhinorrhea present in the nasal passages. The remainder of the examination is unremarkable. Should she be treated with an antibiotic?

THE CLINICAL PROBLEM

Viral upper respiratory tract infections are common in children of all ages. Acute bacterial sinusitis is purported to complicate about 6 to 8% of cases, although the exact incidence is not known.[1,2] Children who attend day care are twice as likely to have sinusitis after an upper respiratory tract infection as those who do not attend day care.[3] In the United States, sinusitis affects about 1% of children each year and accounts for more than $1.8 billion in direct health care expenditures and 20 million prescriptions for antibiotics per year.[4,5]

The two most common predisposing factors for acute bacterial sinusitis are viral upper respiratory tract infection and allergy.[6] Approximately 80% of episodes of acute bacterial sinusitis are preceded by a viral upper respiratory tract infection. An understanding of the natural history of such infections is important to differentiate them from sinusitis. Colds are characterized by nasal obstruction and discharge, with or without sore throat.[7] The nasal discharge is initially clear and watery, becomes thick and mucoid, and is subsequently colored and opaque. Before resolving, the nasal discharge dries or reverses in pattern, becoming watery and clear. Hoarseness and cough may be concurrent or follow the nasal symptoms. Fever is more common in children (up to the age of 8 years) than in adults with upper respiratory infection, and when present, it typically resolves in 1 to 2 days. The infection usually lasts for 5 to 10 days, with symptoms peaking on day 3 to 5.[8] Less than 10% of children with colds have symptoms for more than 10 days, and most of those who do have an improvement in symptoms by day 10.[9] In a study of 1996 children with respiratory symptoms, only 6.5% had symptoms that had not begun to abate at the 10-day mark.[2]

The presentation of acute bacterial sinusitis conforms to one of three patterns.[10] Most frequently, children present with symptoms of upper respiratory tract infection — nasal congestion (or rhinorrhea), cough, or both — that have persisted for more than 10, but less than 30 days, without subsiding. The rhinorrhea may be of any quality (thick or thin, watery, mucoid, or purulent). The cough, which may be wet or dry, occurs in the daytime but is often worse at night; a cough that occurs only at night is more indicative of postnasal drip or reactive airways disease. Because viral upper respiratory tract infections generally begin to abate within 10 days, it is the persistence of symptoms, without improvement, that is the hallmark of this

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KEY CLINICAL POINTS

Acute Bacterial Sinusitis in Children

- In most instances, acute bacterial sinusitis in children follows a viral upper respiratory infection.
- Sinusitis in children has three predictable patterns of presentation: persistent, severe, and worsening symptoms.
- The diagnosis of acute bacterial sinusitis should be made on the basis of the history, generally without the use of imaging studies.
- *Haemophilus influenzae* appears to have become more common and *Streptococcus pneumoniae* less common as causes of acute bacterial sinusitis in children.
- Rates of beta-lactamase production in *H. influenzae* have increased in many geographic areas.
- Studies of the use of antimicrobial agents have had conflicting results, but findings generally support treatment.
- Amoxicillin–clavulanate should be considered as the first-line treatment for sinusitis in children.

presentation. On physical examination, the child may appear only mildly ill. Fever, if present, is low grade. The nasal mucosa is erythematous, and discharge may be visible on the nasal turbinates.

The second pattern is characterized by severe symptoms at onset. Children present with a high temperature (≥38.5°C) of at least 3 to 4 days' duration[11] — a longer period than the 1 to 2 days that is typical of a viral upper respiratory tract infection. Fever is accompanied by rhinorrhea that is purulent (thick, colored, and opaque).

The third pattern is characterized by worsening symptoms after an initial improvement (i.e., a biphasic illness).[12] Worsening symptoms, which typically become manifest about a week after the onset of the illness, include new fever and an increase in nasal discharge, daytime cough, or both.

Complications of sinusitis are infrequent, but they may result from the anatomical proximity of the paranasal sinuses to the brain and orbit. These complications may be extracranial, including periorbital inflammatory edema, subperiosteal abscess, orbital cellulitis, orbital abscess, and Pott's puffy tumor (a subperiosteal abscess of the frontal bone), or intracranial, including subdural empyema, epidural or brain abscess, meningitis, and venous sinus thrombosis.[13] Trials of antibiotic therapy have not been powered to assess whether treatment with antimicrobial agents reduces the rate of complications.

The pathogenesis of sinusitis involves three components: obstruction of the sinus ostia, decreased mucociliary clearance, and the development of viscous secretions. Because the mucosa of the sinuses is directly continuous with the mucosa of the nasal cavity, inflammation of the sinus mucosa is common during a viral upper respiratory tract infection. In most patients this inflammatory response resolves spontaneously, but occasionally, obstruction of the sinus ostia, thickening of secretions, or impairment of the mucociliary apparatus occurs, promoting the conditions needed for bacterial growth.

STRATEGIES AND EVIDENCE

EVALUATION

Acute bacterial sinusitis in children is diagnosed on the basis of the history, with the use of the criteria listed in Table 1.[2,3,14] Imaging studies (plain-film radiography, computed tomography [CT], magnetic resonance imaging [MRI], and ultrasonography) show signs of sinus inflammation but are not recommended in patients with uncomplicated infection, given the low specificity of these studies. A high frequency of abnormal findings has consistently been reported for sinus imaging in patients with uncomplicated viral upper respiratory tract infection.[15-20] For example, in a study in which CT was performed in young adults 48 to 96 hours after the onset of a common cold,[16] abnormal findings (consistent with mucosal inflammation) in the paranasal sinuses were reported in more than 80% of patients. Imaging studies cannot distinguish inflammation caused by viruses from that caused by bacteria.

Table 1. Clinical Criteria for the Diagnosis of Acute Bacterial Sinusitis.

Persistent symptoms
Nasal congestion, rhinorrhea, or cough
≥10 Days' duration without improvement
Severe symptoms
Temperature ≥38.5°C for 3–4 days
Purulent rhinorrhea for 3–4 days
Worsening symptoms
Return of symptoms after initial resolution
New or recurrent fever, increase in rhinorrhea, or increase in cough

Although imaging is not indicated for the purpose of diagnosing bacterial sinusitis, it may be useful in ruling out the diagnosis when the findings are normal.[21] CT or MRI is warranted in patients with symptoms or signs suggesting complicated sinusitis (e.g., severe headache, seizures, focal neurologic deficits, periorbital edema, or abnormal intraocular muscle function) and may show drainable fluid collections within the cranium or the orbit.

ANTIMICROBIAL THERAPY

The role of antibiotic therapy in acute bacterial sinusitis is controversial. Of four randomized, placebo-controlled trials of antimicrobial agents for the treatment of sinusitis in children,[2,14,22,23] two showed no benefit of antibiotic therapy.[22,23] In one of the trials with negative findings, a subtherapeutic dose of cefuroxime axetil was used, and the majority of the patients had symptoms for fewer than 10 days.[23] In the other trial,[22] enrolled children had symptoms for at least 10 days, but many of the children had a history of asthma or allergies (which may have confused the diagnosis and affected the response to treatment), the use of symptomatic treatments was permitted (which may have obscured the benefits of the study drug), and the doses of amoxicillin and amoxicillin–clavulanate that were used may have been too low to eradicate *Streptococcus pneumoniae*. The major outcome measure was a score based on symptoms rather than an a priori definition of treatment failure or cure.

A more recent trial compared the use of high-dose amoxicillin–clavulanate with placebo in 58 children between 1 and 10 years of age who had persistent, worsening, or severe symptoms. On assessment 14 days after the start of therapy, patients randomly assigned to active treatment (90 mg of amoxicillin and 6.4 mg of clavulanate per kilogram of body weight per day, administered in two doses) were less likely to have treatment failure (14%, vs. 68% with placebo); the number of patients who would need to be treated to prevent one case of treatment failure was 3 (95% confidence interval, 1.7 to 16.7). Adverse events (most frequently, diarrhea) were more common in children receiving the antibiotic than in those receiving placebo (44% vs. 14%) and resulted in discontinuation of antibiotic therapy in 3 of 28 (11%) children.[2]

The fourth trial compared amoxicillin (40 mg per kilogram per day, administered in three doses), amoxicillin–clavulanate (40 mg of amoxicillin and 10 mg of clavulanate per kilogram per day, administered in three doses), and placebo. This trial showed a benefit in both groups receiving antibiotic therapy. Cure was noted by day 3 in 45% of the children receiving an antibiotic and 11% of those receiving placebo and by day 10 in 65% and 40%, respectively. The cure rates for amoxicillin (67%) and amoxicillin–clavulanate (64%) were not significantly different. However, this study was conducted before the introduction of pneumococcal conjugate vaccine.[14]

Selecting an appropriate antimicrobial agent for the treatment of sinusitis requires knowledge of the probable infecting pathogens and their resistance patterns. Two studies conducted decades ago involving maxillary sinus aspiration in children presenting with sinus symptoms of 10 to 30 days' duration[24,25] identified *S. pneumoniae* as the predominant bacterium (detected in 40% of all isolates), followed by nontypable *Haemophilus influenzae* and *Moraxella catarrhalis* (each detected in 20% of all isolates), and, less frequently, other bacteria (group A streptococcus, group C streptococcus, *Eikenella corrodens,* peptostreptococcus, and alpha-hemolytic streptococcus). Respiratory viruses, including parainfluenza, adenovirus, rhinovirus, and influenza virus, were isolated infrequently with the use of traditional viral culture.[25,26]

No known recent studies of sinus aspiration have been conducted to determine whether the microbiologic nature of acute bacterial sinusitis has changed in the past three decades.[24] Culture of fluid from the middle ear (which is a paranasal sinus) obtained by means of tympanocentesis from children with acute otitis media may serve as a

surrogate for culture in the other paranasal sinuses.[27] Studies conducted within the past 10 years or so have documented a decrease in the relative proportion of cases of acute otitis media caused by *S. pneumoniae,* a finding attributable to the introduction of the 7-valent and 13-valent pneumococcal conjugate vaccines (PCV7 and PCV13, respectively).[28-30] The rate of isolation of nontypable *H. influenzae* has increased correspondingly.[28]

The choice of antibiotic must take into account not only the probable infecting flora but also resistance patterns, which vary over time and according to geographic location. Rates of resistance to penicillin among *S. pneumoniae* isolates are typically 10 to 15% but may be as high as 50% in some areas.[31,32] Similarly, rates of beta-lactamase production among *H. influenzae* isolates range from 10 to 68%[33-35] (and Glode M: personal communication). *M. catarrhalis* produces beta-lactamase nearly 100% of the time. The resistance of sinus pathogens to macrolides is increasing. The rates of resistance to azithromycin range from 22 to 63% for *S. pneumoniae*, and resistance rates as high as 100% have been reported for *H. influenzae*.[30,31,33,36,37] Approximately one quarter of all *H. influenzae* isolates and half of *S. pneumoniae* isolates show resistance to trimethoprim–sulfamethoxazole.[33] The fluoroquinolones, such as levofloxacin and moxifloxacin, have a high level of activity against both *S. pneumoniae* and *H. influenzae* when isolated from respiratory specimens, but these medications are not routinely recommended because of concerns about toxicity, cost, and emerging resistance.[31,32] Linezolid has excellent activity against *S. pneumoniae,* including penicillin-resistant strains, but it lacks activity against *H. influenzae* and *M. catarrhalis*.[32]

Amoxicillin–clavulanate, typically administered in doses of 90 mg per kilogram per day, has the most comprehensive in vitro coverage of the bacteria that cause sinusitis and should be considered first-line treatment for acute bacterial sinusitis, particularly since rates of beta-lactamase–producing *H. influenzae* are increasing in many geographic areas. Amoxicillin alone may be used as an alternative but should be administered in doses of 90 mg per kilogram per day in areas where penicillin-nonsusceptible infection is endemic and resistance rates are 10% or higher in children at increased risk for resistant pneumococci (children younger than 2 years of age, those attending day care, and those who have received an antibiotic within the preceding month).

Other antibiotics have not been systematically evaluated for the treatment of acute bacterial sinusitis in children but are used as alternatives to those described above. Cephalosporins such as cefuroxime axetil, cefpodoxime, or cefdinir may be used, but they are not as comprehensive in coverage as amoxicillin–clavulanate. Azithromycin and clarithromycin are no longer recommended for the treatment of sinusitis, owing to high rates of resistance among both *S. pneumoniae* and *H. influenzae* isolates. For the rare patient with severe allergy to penicillins and cephalosporins, levofloxacin (the only respiratory fluoroquinolone available in a liquid formulation) should be considered, although it has not been approved by the Food and Drug Administration for this indication in children. If treatment with amoxicillin–clavulanate fails, either levofloxacin or a combination of clindamycin with cefixime or linezolid with cefixime may be offered. (The antimicrobial agents used to treat acute bacterial sinusitis are presented in Table 2.)

Data are lacking to compare the effectiveness of various antibiotics in the treatment of acute bacterial sinusitis in children and to determine the most effective duration of treatment. Professional guidelines recommend treatment for 10 to 14 days, or until the patient is free of symptoms plus another 7 days.[11]

SYMPTOMATIC THERAPY

The limited data available from randomized trials have not shown that nasal saline washes or sprays provide substantial relief from symptoms and have shown that intranasal glucocorticoids provide only slight relief (i.e., too modest for their use to be routinely recommended).[38,39] Antihistamines and decongestants have been shown to be of no benefit in relieving symptoms of sinusitis in children and may have clinically significant toxicity.[40,41]

PREVENTION

Prevention of the antecedent viral infection or of colonization by pathogenic bacteria would be expected to prevent acute bacterial sinusitis. Whereas rates of otitis media have decreased in association with the increasing use of influenza vaccination[42] and with the introduction of the pneumococcal conjugate vaccine, data are lack-

Table 2. Antimicrobial Agents Used in the Treatment of Sinusitis in Children.*

Drug	Dose	Adverse Events	Comments
Amoxicillin	40–90 mg/kg of body weight/day, administered in two doses	Diarrhea, rash	Higher dose should be used when there is a risk of pneumococcal resistance
Amoxicillin–clavulanate†	40–90 mg of amoxicillin/kg/day, administered in two doses	Diarrhea, rash	Higher dose should be used when there is a risk of pneumococcal resistance
Cefdinir	14 mg/kg/day, administered in one or two doses	Diarrhea, rash	
Cefixime	8 mg/kg/day, administered in one dose	Diarrhea, rash	
Cefpodoxime	10 mg/kg/day, administered in two doses	Diarrhea, rash	
Cefuroxime axetil	30 mg/kg/day, administered in two doses	Diarrhea, rash	
Clindamycin (with cefixime)	30–40 mg/kg/day, administered in three doses	Diarrhea	Poor palatability in children
Levofloxacin	16 mg/kg/day, administered in two doses, 12 hr apart	Musculoskeletal discomfort	Resistance may develop rapidly; not approved by the FDA for this indication
Linezolid (with cefixime)	20–30 mg/kg/day, administered in two or three doses	Serotonin syndrome, myelosuppression, rash, lactic acidosis, neuropathy	Interactions with selective serotonin inhibitors and high-tyramine foods; not approved by the FDA for this indication

* FDA denotes Food and Drug Administration.
† Amoxicillin–clavulanate is recommended as a first-line treatment.

ing to show similar declines in office visits or prescriptions for sinusitis in children.[43]

AREAS OF UNCERTAINTY

The precise role of viral infection in the pathogenesis of acute bacterial sinusitis (as an antecedent event predisposing the patient to bacterial infection or as a concurrent infection) remains unclear. Whereas most episodes of acute bacterial sinusitis are believed to be preceded by viral upper respiratory tract infection, sinus-puncture studies have yielded viruses in less than 10% of patients.[25,26] However, in most studies, samples have been obtained late in the course of illness (7 to 14 days after the onset of symptoms), when the viral yield would be lower, and the techniques used to identify the viruses have been much less sensitive than nucleic acid amplification.

It is uncertain whether *Staphylococcus aureus* plays an etiologic role in acute sinusitis. Although *S. aureus* has been identified in cultures obtained endoscopically in children, it has not been recovered from cultures obtained by means of sinus aspiration[24,25]; this discrepancy may be explained by contamination of endoscopically obtained cultures with nasal flora. Nonetheless, *S. aureus* has been identified as a pathogen in the complications of sinusitis in children.

Although our own data support the use of antibiotics in the treatment of acute bacterial sinusitis,[2,14] data from randomized trials of antibiotic therapy are inconsistent and limited. In addition, the most effective duration of treatment for acute bacterial sinusitis in children has not been investigated systematically.

GUIDELINES

The Infectious Diseases Society of America (IDSA) has recently published recommendations for the management of acute bacterial sinusitis.[44] The recommendations in this article are generally consistent with these guidelines. Prompt treatment is recommended for children who meet criteria suggestive of acute bacterial sinusitis (Table 1). High-dose amoxicillin–clavulanate (90 mg per kilogram per day, administered in two doses) is recommended as first-line therapy for children in regions where penicillin-nonsusceptible *S. pneumoniae* strains are endemic and resistance rates are 10% or higher, those in day care, those younger

than 2 years of age, and those who have been hospitalized or treated with antibiotics in the past month. If these risk factors are not present, standard-dose amoxicillin–clavulanate (40 mg per kilogram per day, administered in two doses) is recommended. Macrolides and trimethoprim–sulfamethoxazole are not recommended because of the high rates of resistance in the United States. Levofloxacin is recommended for children with a history of type I hypersensitivity reaction to penicillin. The recommended duration of treatment with amoxicillin–clavulanate or levofloxacin is 10 to 14 days in children.

CONCLUSIONS AND RECOMMENDATIONS

The presentation of the child described in the vignette — rhinorrhea and cough for 12 days — is consistent with acute bacterial sinusitis. The diagnosis of sinusitis should be made on the basis of clinical criteria; imaging is not routinely indicated. Although the criterion of 10 or more days of symptoms is not absolute (and is infrequently met in cases of viral upper respiratory tract infection), in the majority of children with viral infection, symptoms will have resolved or diminished by this time. Given evidence, albeit inconsistent, that antimicrobial therapy for acute bacterial sinusitis significantly increases the likelihood of cure within 10 days, we would recommend antibiotic therapy for this child; amoxicillin–clavulanate would be the first choice and is consistent with IDSA guidelines. Although the optimal duration of therapy is not known, a course of 10 to 14 days is adequate in most patients. Gastrointestinal symptoms are a common side effect but are usually mild and self-limited. Neither antihistamines nor decongestants are recommended because they are unlikely to be of benefit and may have adverse effects.

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Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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