MEDICAL MANAGEMENT OF ACUTE BACTERIAL SINUSITIS

RECOMMENDATIONS OF A CLINICAL ADVISORY COMMITTEE ON PEDIATRIC AND ADULT SINUSITIS

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Acute sinusitis is commonly encountered in clinical practice and treated in the primary care setting. The clinician should recognize the subtle clinical presentation of acute bacterial sinusitis and initiate appropriate, aggressive treatment. Other upper respiratory tract disorders can confound the accurate diagnosis and appropriate treatment of sinusitis. Variable patterns of microbial resistance and antibiotic susceptibility and the dissociation between in vitro findings and clinical efficacy are a treatment challenge. This report is a comprehensive review of the pathophysiology and diagnosis of acute sinusitis, infectious agents, treatment methods, antibiotic resistance patterns, and costs associated with the management of sinusitis. Treatment algorithms are presented for adult and pediatric sinusitis.

KEY WORDS — amoxicillin, amoxicillin-clavulanate, antibiotic resistance, antimicrobials, cephalosporin, fluoroquinolone, *Haemophilus influenzae*, *Moraxella catarrhalis*, sinusitis, *Streptococcus pneumoniae*, trimethoprim-sulfamethoxazole

INTRODUCTION

Sinusitis is a common disorder that affects more than 30 million individuals each year in the United States.[1] About 90% of patients will visit their primary care physician for sinusitis treatment.[2] It is important for primary care physicians to be attentive to this condition because its incidence appears to be on the rise.[2] Prompt, effective therapy is required to reduce lost work time for adults and to permit children to return to school, allowing parents to return to work.[3] Antimicrobial resistance patterns have changed to create increasingly complicated problems with antimicrobial therapy.[4]

There are many pitfalls in accurately diagnosing acute bacterial sinusitis, one being overlaps with other upper respiratory tract diagnoses (allergies, viral infections, idiopathic rhinitis, fungal disease, neoplastic processes). The diagnosis of sinusitis is often presumptive and treatment is empirical, which presents further challenges to clinicians. The emergence of resistance and variable antibiotic susceptibilities of causative bacteria poses a greater challenge to antibiotic selection. Because sinusitis significantly impacts quality of life, clinicians should be aware of the trends in diagnosis and treatment of the acute condition.[5]

DEFINITION AND PATHOPHYSIOLOGY

Sinusitis encompasses a spectrum of acute and chronic, neutrophilic and eosinophilic, nonallergic and allergic inflammatory processes.[6] Bacterial sinusitis is an inflammation of the paranasal sinus mucosa caused by bacterial overgrowth in a closed cavity. This disorder is also called rhinosinusitis, because the nasal epithelium is continuous with the mucosa that lines the paranasal sinuses and the disease can affect both sites.[7] Viral or allergic rhinitis typically precedes sinusitis, and sinusitis without rhinitis is rare.[4,8] Many factors may predispose an individual to sinusitis (Table 1). Recent evidence shows that viral upper respiratory tract infections (URTIs) and pharyngeal colonization with group A streptococci predispose children to acute bacterial sinusitis.[9] It may be appropriate to select antibiotics that are also effective against group A streptococci, because *Streptococcus pyogenes* may be a concurrent infection in 15% to 20% of children.[9]

The maxillary, frontal, ethmoid, and sphenoid sinuses all drain into the nasal cavity through the ostia, which are approximately 1 to 3 mm in diameter (Fig 1). Obstruction of this narrow space may set up an environment for bacterial pathogens to colonize. Antibiotic use for acute obstruction is generally not indicated; however, if the obstruction persists for 7 to 10 days, secondary bacterial infection is likely. In acute bacterial sinusitis, a single bacterial species is responsible for the infection; however, multiple bacterial isolates were cultured in 26% and 30% of cases

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TABLE 1. FACTORS PREDISPOSING TO SINUSITIS

Prior upper respiratory tract infection

Concurrent group A streptococcal infection

Allergic rhinitis

Environmental pollutants (smoke)

Dental infections or extractions

Hormonal changes

Iatrogenic factors (mechanical ventilation, nasogastric tubes, nasal packing, dental procedures)

Anatomic variations (tonsillar and adenoid hypertrophy, deviated septum, nasal polyps, cleft palate)

Swimming

Immunodeficiency

Secretory disturbances (cystic fibrosis)

Immotile cilia syndrome

Abnormal mucociliary clearance secondary to ciliary structural abnormalities (Kartagener's syndrome)

Bronchiectasis

Asthma or acetylsalicylic acid–asthma–polyposis triad

Immature immune system

Adenoidal hypertrophy

in 2 studies, respectively.[10]

In addition to obstruction caused by inflammatory edema of the mucosa, viral and bacterial inflammation also decreases mucociliary activity, further compromising natural host defenses. Impaired ciliary transport results in stagnation of secretions, decreased pH, and lowered oxygen tension, providing a perfect medium for bacterial multiplication.[11]

Sinusitis is classified on the basis of duration of symptoms and anatomic location. Acute sinusitis symptoms last as long as 4 weeks.[12] Subacute sinusitis has minimal to moderate symptoms that are present for 4 to 12 weeks. Chronic sinusitis persists for more than 12 weeks and often has a pathophysiology that differs from that of acute sinusitis.[12] Chronic sinusitis represents an ongoing inflammation characterized by eosinophilia. The inciting agents of chronic sinusitis have been difficult to identify or prove.[4] Repeated damage of the mucosa in this condition causes loss of the normal state of sterility.[10] Recurrent sinusitis is defined as 4 or more episodes in 1 year, each episode lasting more than 7 days, with complete resolution between episodes.

The pathophysiology of sinusitis in children may be slightly different. Until recently, physicians assumed that sinuses were absent in infants and young children and often overlooked sinusitis in the pediatric population.[13] The ethmoid and maxillary sinuses are present and clinically significant at birth; however, the other sinuses develop more slowly. The sphenoid sinus develops between 3 and 7 years of age, and the frontal sinuses develop by 12 years of age. The sinuses continue to develop during childhood and adolescence.[14] In addition, the immune system is immature in children, making host reduction of bacterial load more difficult.[8] There is a lack of agreement about the clinical definition of sinusitis in children.[15]

EPIDEMIOLOGY, PREVALENCE, AND ECONOMICS OF SINUSITIS

Each year, approximately 16% of adults in the United States receive diagnoses of sinusitis. The incidence of sinusitis is higher in the Midwest and South, compared with the Northeastern and Western regions of the United States.[4] Rates of sinusitis are higher in the fall, winter, and spring months.[16] A National Center for Health Statistics annual survey estimated that 1 in 5 Americans has symptoms related to sinus disease and nasal allergies but does not seek medical attention.[17] Because many individuals do not seek medical help for this condition, the actual number of individuals affected may be much higher. Those who seek treatment account for an estimated 16 million office visits per year.[6,18] More than $2 billion is spent

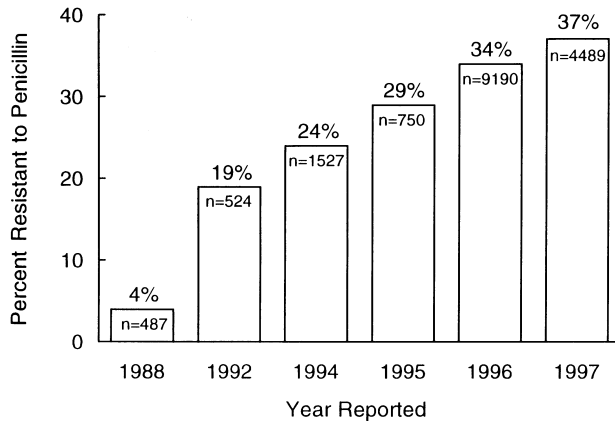
Fig 1. Diagram of paranasal sinuses.
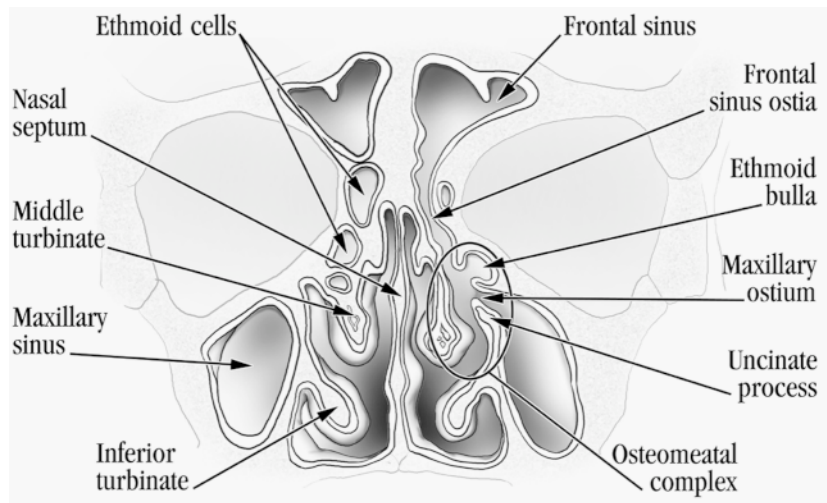
Fig 2. Increasing trend in *Streptococcus pneumoniae* penicillin resistance. Resistance is defined as either intermediate resistance (minimal inhibitory concentration of ≥ 0.12 µg/mL) or high resistance (minimal inhibitory concentration of ≥ 2 µg/mL).

annually for over-the-counter medications for sinusitis.[18] The National Ambulatory Medical Care Survey found sinusitis to be the fifth leading diagnosis for which providers prescribed an antibiotic.[19]

Because nasal symptoms are some of the most common complaints brought to primary care physicians, patients need to be informed that nonbacterial causes are most often the basis for symptoms such as rhinitis, nasal congestion, facial pressure, headaches, and postnasal discharge. Acute viral URTIs, seasonal allergic rhinitis, perennial allergic rhinitis, vasomotor rhinitis, and rhinitis medicamentosa have symptoms that overlap with acute bacterial sinusitis and are often a cause for misdiagnosis.[7] Physician compliance with patients' expectation of an antibiotic can result in indiscriminate antibiotic use. Studies show that 18% to 60% of patients with colds are prescribed antibiotics.[20-22] A Canadian survey found that approximately 50% of antibiotics were not indicated on the basis of evidence-based guidelines.[23] The reasons for overprescribing include physicians' education and experience, patient expectations, and economics.[24] However, studies of overprescribing may not have considered antibiotic use for prophylactic therapy, severity of illness, follow-up arrangements, or patient income variables.[25,26]

Viral rhinosinusitis is a more likely cause of nasal symptoms than any bacterial origin.[27,28] Viral rhinosinusitis occurs more often than bacterial sinusitis and does not require antibiotic treatment.[29] Although allergic rhinitis may be a predisposing factor in bacterial rhinosinusitis, it has not been clearly shown to cause bacterial rhinosinusitis in adults, and there is only a slight correlation in children.

Rhinosinusitis in children is a multifactorial disease. As the child becomes older, several predispos-

ing factors change.[30] About 10% to 20% of children actually have allergic rhinitis, which may be present all year. Children 2 to 5 years of age average 6 to 8 URTIs per year.[31,32] Approximately 5% to 10% of these URTIs may become complicated by acute bacterial sinusitis.[33] Children in day-care centers have more frequent and longer-lasting respiratory tract infections because of superinfection.[34,35] Anatomic variations in children typically do not contribute to the prevalence of pediatric sinusitis.[36]

PATHOGENS IN SINUSITIS

The causative organisms of acute bacterial sinusitis are similar to those of acute otitis media. They include *Streptococcus pneumoniae* (30% to 40% of clinical isolates), *Haemophilus influenzae* (20% to 30%), *Moraxella catarrhalis* (12% to 20%), and *Streptococcus pyogenes* (up to 3%).[37] Other pathogens, found less frequently, include other *Streptococcus* species, *Staphylococcus aureus*, *Neisseria* species, and gram-positive and other gram-negative bacilli. Fungi are most commonly observed in immunocompromised and diabetic individuals. Anaerobic infections may occur in chronic sinusitis or with dental disease.[12]

Clinical studies in children with sinusitis are rare, because of the difficulties in diagnosing sinusitis in this age group. In the few pediatric studies published, the pathogens cultured from children with acute sinusitis and subacute sinusitis are similar to those of adults.[3,10] The predominant pathogens isolated from pediatric patients with chronic sinusitis are *S pneumoniae*, *M catarrhalis*, *H influenzae*, and anaerobes.[38-41]

ANTIBIOTIC RESISTANCE

The incidence of the bacterial species causing sinusitis has not changed in more than 4 decades; however, antimicrobial susceptibilities have changed within the past 2 decades.[12] Before 1980, more than 99% of pneumococcal strains were susceptible to penicillin. Recently, the prevalence of penicillin-resistant pneumococci has increased dramatically worldwide and shows a nearly twofold regional variation within the United States, approaching 33% to 58% of clinical isolates.[42,43] Data from US national surveillance studies showed a 4% resistance rate in the 1980s, which increased to 37% in 1997 (Fig 2).[44-50]

At least one third of *H influenzae* isolates and the majority of *M catarrhalis* isolates are β-lactamase–producing. Before 1972, *H influenzae* was almost uniformly susceptible to ampicillin. Since then, β-lactamase–producing strains resistant to ampicillin represent 30% to 40% of isolates.[51] *Moraxella catarrhalis*
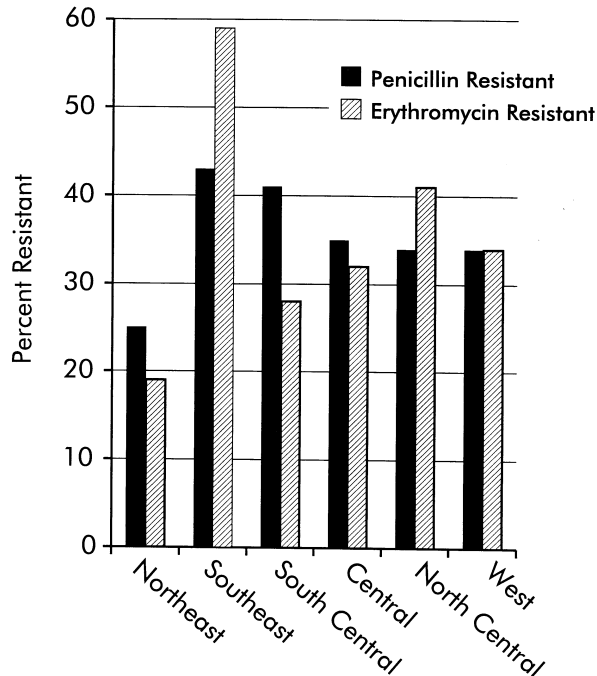
Fig 3. Prevalence of intermediately and highly resistant strains of *Streptococcus pneumoniae* in United States by region, September 1998 to February 1999.

was once uniformly susceptible to all agents, but is now commonly resistant. Wallace et al[52] reported a high rate of *M catarrhalis* resistance (>75%) due to the production of β-lactamase.[52] Doern et al[53] and Thornsberry et al[50] reported similar high rates of β-lactamase production in isolates of *M catarrhalis*: 95.3% and 92.7%, respectively.

The overuse of antibiotics, inappropriate dosing, and the use of broad-spectrum antibiotics as first-line treatment have contributed to the rising incidence of drug-resistant strains of bacteria. Resistance will continue to emerge and make our first-line agents less useful. Some penicillin-resistant strains display multidrug resistance to trimethoprim-sulfamethoxazole (TMP-SMX), macrolides, and some cephalosporins.

It is difficult to predict emerging resistance patterns. Antibiotic use in children is possibly a factor in emerging resistance, especially in day-care settings.[54] Several studies have shown that there are substantial rates of multidrug-resistant pneumococci among children in day-care settings.[55-58] Currently, it is estimated that greater than 50% of pneumococcal isolates from children in rural and urban day-care settings are resistant to penicillin.[55]

It is important for physicians to know the resistance patterns in their specific community. Four percent to 48% of *S pneumoniae* isolates are resistant to penicillin, depending on geographical area.[59] Geographical resistance patterns of *S pneumoniae*, *H in-*

fluenzae, and *M catarrhalis*, the 3 most common upper respiratory tract pathogens (a total of 4,979 clinical isolates), were studied in 52 independent and hospital laboratories across the United States from September 1998 to February 1999.[60] The standards and guidelines of the National Committee for Clinical Laboratory Standards (NCCLS) were used for test methods. The United States was divided into 6 regions (Fig 3). Approximately one fourth of the *S pneumoniae* isolates tested against penicillin were resistant. In the Northeast and in the West, penicillin resistance rates were significantly lower. The rates of erythromycin resistance were similar to the rates of penicillin resistance. Although high resistance rates were noted across the country, significantly higher rates were noted in the Southeast. Thirty-one percent of *H influenzae* isolates produced β-lactamase. Ten strains were β-lactamase–negative and showed intermediate resistance to ampicillin. *Haemophilus influenzae* showed consistently high resistance rates to ampicillin across all regions and showed lower resistance rates to TMP-SMX, except in the Southeast. The resistance rates and positive β-lactamase production were consistent and alarmingly high across all regions, reaching 87% to 96% for *M catarrhalis*.

There is a direct correlation between β-lactamase production and the prior use of β-lactam antibiotics.[61] β-lactamase–producing bacteria and penicillin-resistant *S pneumoniae* appear to be more prevalent in the winter months than in the summer and fall months. In a study of patients from a suburban area in Washington, DC, the percentage of patients with oropharyngeal colonization with β-lactamase–producing organisms gradually increased from September to April and slowly decreased from April to August.[61]

Brook and others[62-64] have shown that the administration of some β-lactam antibiotics select β-lactamase–producing organisms in the respiratory tract. These organisms can spread within a family setting to other household members.[63] Prophylactic use of amoxicillin also selects penicillin-resistant organisms.[61]

INTERFERENCE PHENOMENON

The use of wide-spectrum antimicrobial agents may alter the normal upper respiratory tract flora. The use of such antibiotics may contribute to persistence of infection by inhibiting the nonpathogenic organisms in the upper respiratory tract that generally interfere with the growth of potential pathogens.[65,66] A comparative trial evaluated the effect of amoxicillin-clavulanate and cefprozil on the nasopharyngeal bacterial flora in children treated for acute otitis media.

Both agents were equally effective in eradicating the pathogenic organisms *S pneumoniae*, *H influenzae*, and *M catarrhalis*. Therapy with amoxicillin-clavulanate resulted in a significant decrease in the number of interfering, nonpathogenic bacteria, and cefprozil had only a minimal effect.[67] The nonpathogenic bacteria included α-hemolytic streptococci, *Prevotella melaninogenica*, and *Peptostreptococcus anaerobius*. The number of these interfering organisms was reduced at the end of therapy, from 50 to 11 after amoxicillin-clavulanate therapy, and from 50 to 42 after cefprozil therapy (p < .001). However, long-term follow-up was not performed in this study.

These interfering organisms are relatively resistant to second- and third-generation cephalosporins, but are susceptible to amoxicillin-clavulanate. The impact of antibiotics on normal flora that possess interfering capability toward pathogens needs further evaluation.

β-Lactamase–producing bacteria in the respiratory tract protect or shield penicillin-susceptible pathogens from inhibition by penicillin or amoxicillin.[68] β-Lactamase activity was detected in 12 sinus aspirates that harbored β-lactamase–producing bacteria in patients in whom antimicrobial therapy failed.[69]

DIAGNOSIS

Intranasal cultures are not indicative of the bacterial origin of acute sinusitis. The diagnosis of acute sinusitis is often difficult and is based on a careful, thorough history and physical examination. Although sinus aspiration and culture is the "gold standard" of diagnosis, the procedure is painful and may lead to iatrogenic infection. The majority of patients who visit a primary care physician for respiratory symptoms are likely to have a viral rather than a bacterial cause of sinusitis.[70,71]

Differentiating viral rhinosinusitis from bacterial sinusitis is often difficult, because viral rhinosinusitis often precedes bacterial sinusitis. In general, symptoms of bacterial sinusitis worsen after 5 days, persist for at least 10 days, and are more severe than those of viral disease.[72] About 0.5% of URTIs progress to sinusitis.[73,74] However, viral symptoms that persist for more than 7 days often establish an environment suitable for the development of bacterial infections and may predispose the patient to bacterial sinusitis.

The overall clinical impression is a more accurate diagnostic predictor of sinusitis than any single diagnostic predictor.[75,76] According to the Task Force on Rhinosinusitis of the American Academy of Otolaryngology–Head and Neck Surgery, diagnosis of acute sinusitis depends on the presence of at least 2 major diagnostic factors or 1 major factor and 2 minor fac-

TABLE 2. DIAGNOSTIC FACTORS PREDICTIVE OF SINUSITIS

Major factors
Facial pain or pressure (requires another major factor for diagnosis)
Facial congestion or fullness
Nasal obstruction
Nasal purulence or discolored postnasal discharge
Hyposmia or anosmia
Fever (acute sinusitis only)
Minor factors
Headache
Halitosis
Fatigue
Dental pain
Cough
Ear pain, pressure, or fullness
Fever (nonacute sinusitis)
Based on data from Lanza and Kennedy.[72]

tors (Table 2).[72] The number of diagnostic factors correlates with the likelihood that a bacterial infection is present.

A retrospective analysis found that family practice physicians relied on only 4 factors (sinus tenderness, facial pressure, postnasal drainage, and discolored postnasal drainage) to differentiate sinusitis from URTIs.[77] However, no particular sign or symptom is sensitive and specific for sinusitis.[75,78]

Relying on poor clinical predictors (ie, imprecise signs and symptoms) has significant implications for antibiotic use. Physicians need to evaluate and consider multiple diagnostic factors in sinusitis. Lindbaek et al[79] found the 4 symptoms and signs associated with a computed tomography (CT)–confirmed diagnosis of acute sinusitis to be 1) 2 phases in the illness history, 2) purulent rhinorrhea, 3) purulent secretions in the cavum nasi, and 4) an erythrocyte sedimentation rate greater than 10 mm. If 3 of these 4 signs and symptoms were present, the diagnosis had a specificity of 81% and a sensitivity of 66%. Although this sensitivity is higher than that of any individual clinical finding, the specificity is lower than that of maxillary edema (99%) or temperature greater than 38°C (89%).

Other complaints that may increase the probability of correctly diagnosing sinusitis include a recent prolonged URTI, a lack of response to decongestants, nasal airway obstruction, facial pain and pressure, sore throat, decreased sense of smell, and edema of the eyelid or chemosis.[80] In adults, purulent postnasal discharge and facial pain over the affected sinus that worsens with movement or percussion are cardinal symptoms.[81] Visualization of purulent nasal drainage on examination may be a strong indicator of acute sinusitis.[76] However, purulence does not differenti-

TABLE 3. VALUE OF SPECIFIC HISTORY, EXAMINATION, AND LABORATORY TEST PARAMETERS IN
INITIAL DIAGNOSIS OF ACUTE SINUSITIS

Parameter	Importance
Patient history	
"Cold" present for more than 7 to 10 days	Significantly important
Unusually severe upper respiratory tract complaints	Significantly important
Fever	Significantly important
Mucopurulent discharge (>7 days)	Significantly important
Pain in upper teeth	Significantly important
Lack of response to over-the-counter decongestants	Significantly important
Dull headache	Variable importance*
Clinical assessments	
Unilateral or bilateral tenderness in midface region	Significantly important
Inspection of nasal mucosa	Significantly important
Facial tenderness	Significantly important
Intranasal pus	Significantly important
Purulent postnasal mucus in pharynx	Significantly important
Transillumination	Not significantly important
Diagnostic tests	
Radiographs (Waters' view)	Variable importance*
Radiographs (3 views)	Not significantly important
Sinus aspiration, when indicated	Significantly important
Computed tomography†	Not significantly important
Anterior rhinoscopy	Significantly important
Ultrasound	Not significantly important
Magnetic resonance imaging	Not significantly important
Fiberoptic nasal endoscopy	Variable importance*
Nasal mucus smear	Not significantly important
Immunologic screen	Not significantly important
Cultures from sinus puncture (when indicated)	Significantly important
Erythrocyte sedimentation rate	Not significantly important

*Important only in context of other signs, symptoms, and patient history in whole picture of clinical assessment.

†Chronic infection or complications pending.

ate between a viral origin and a bacterial origin.

Anterior rhinoscopy is very important and can be performed with a nasal speculum or otoscope. The use of a topical decongestant before the examination may improve the field of view. The examination should include viewing the turbinates and septum, evaluating the quality of the mucus, and determining the presence of polyps and bleeding.

Symptoms in children are different from those in adults and are difficult to distinguish from those of the common cold or vasomotor rhinitis. They are more nonspecific and may include rhinorrhea, nasal congestion or obstruction, fever, purulent anterior or posterior nasal discharge, snoring, mouth breathing, feeding problems, bad breath, cough, and hyponasal speech.[13,15] The most common complaints are cough and nasal discharge. The classic signs and symptoms found in adults (eg, facial pain and headache) are rare.[82] Pediatric acute sinusitis must be differentiated from allergic rhinitis, which is characterized by continuous stuffiness, sneezing, itchy eyes, and a family history of atopy. Adenoidal hypertrophy or a severely deviated nasal septum may also contribute to

symptoms. The presence of a foreign body, asthma, or neoplasm must be ruled out.[13]

Further diagnostic testing and imaging should be performed for atypical cases and treatment failures. No imaging studies are recommended for the routine diagnosis of uncomplicated sinusitis presented to the primary care physician.[83] The diagnostic value of sinus radiographs is limited by poor sensitivity and specificity. Radiologic evidence of sinusitis is frequently found in patients with viral rhinitis.[84] The Waters' view may offer the simplest demonstration of fluid accumulation in the maxillary sinus. Although the presence of opacification or air-fluid levels in the sinuses is fairly predictive of bacterial infection, it is seen in only 60% of patients with acute sinusitis.[85] If mucosal thickening is included as an indication of sinusitis, the specificity can be as low as 36%.[86]

Researchers conclude that transillumination has limited diagnostic use and depends on the clinician's skill level.[75] As a single finding, transillumination cannot be relied on to confirm or rule out the diagnosis.[87] Ultrasound also has limited diagnostic value.

A CT scan should be reserved for patients who re-

TABLE 4. RISK FACTORS PROMPTING USE OF
SECOND-LINE AGENT

Antibiotic use in past month
Resistance common in community
Failure of first-line agent
Infection in spite of prophylactic treatment
Smoker in family
Child in day-care facility
Younger than 2 years of age
Patient history
Allergy to penicillin or amoxicillin
Frontal or sphenoidal sinusitis
Complicated ethmoidal sinusitis
Presentation with protracted (>30 days) symptoms

spond inadequately to medical therapy, have numerous bacterial infections throughout the year, or have a history of polyposis. Most patients with a viral URTI who undergo a CT scan will demonstrate evidence of sinusitis, and therefore, the value of CT scanning in diagnosis is questionable. However, CT scanning is useful in identifying the underlying cause of chronic infection and in identifying the sinuses involved and any complications that may exist. The CT scans should be performed in a coronal view, and a limited series is usually adequate. Contrast enhancement is not recommended unless there is a central nervous system complication. Table 3 presents the value of specific history, examination, and laboratory test parameters in the initial diagnosis of acute sinusitis.

ANTIMICROBIAL THERAPY

Although 40% of sinusitis patients will recover spontaneously, antibiotics are indicated in the treatment of correctly diagnosed acute sinusitis.[4,37,51] Hueston et al[77] noted that 3 of 4 randomized trials support the use of antibiotics in treating acute sinusitis. Sinusitis is treated empirically because of the invasive nature of culturing the paranasal sinuses. Comparative trials have shown minimal evidence of the superiority of one antibacterial agent over another.[16,88] Effective antibiotic therapy often produces a more rapid resolution of symptoms.[7,89]

The goal of treatment is to arrest the acute infection before it progresses and to prevent serious sequelae (eg, facial osteomyelitis, cavernous sinus thrombosis, meningitis, orbital cellulitis or abscess, or brain abscess).[90,91] Most importantly, appropriate use of antibiotics may decrease the rate of complications, as well as prevent the progression of acute sinusitis to chronic sinusitis through a more rapid reduction of tissue edema and bacterial contamination and the reestablishment of drainage and ventilation of the sinus cavity. Treatment is thought to prevent permanent mucosal damage.[80] Clayman et al[92] found the

rate of intracranial complications from acute sinusitis to be 3.7% in adults. Lerner et al[93] found a similar incidence (3.0%) in children. Despite adequate antibiotic treatment, the mortality rate (30%) and the morbidity rate (60%) from cavernous sinus thrombosis remain high in adults and slightly better in children.[94]

Treatment of bacterial sinusitis usually begins with an inexpensive first-line agent (eg, amoxicillin or TMP-SMX). A recent analysis of in vitro data suggests that current doses of amoxicillin may not be adequate for eradication of intermediately and fully resistant *S pneumoniae*. It is recommended that the amoxicillin dose be doubled (up to 80 to 90 mg/kg per day; maximum of 3 g/d), especially in areas in which resistance to *S pneumoniae* is high. The clinical benefit of using higher doses of amoxicillin still needs to be evaluated in clinical trials.[95] In many geographic areas, the resistance of *S pneumoniae* to TMP-SMX is higher than that to penicillin. Resistance of *H influenzae* to TMP-SMX has increased significantly in recent years.[96] Second-line agents should be used when resistant pathogens are suspected. Table 4 lists the risk factors.

Choosing a second-line antibiotic depends on proven clinical efficacy, resistance patterns, dosing schedules, the adverse events profile, the potential for compliance, knowledge of patient allergies, the previous response history, the physician's experience with agents, and the cost-benefit ratio. Antibiotic choice based on pharmacokinetic properties alone may be misguided. Although the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) have been the gold standards for measuring drug activity, they provide only partial information. The MIC and MBC are useful predictors of drug-organism interaction in a static system, but they do not provide information on the time course of microbial exposure to an antibiotic.[97] For β-lactam antibiotics, vancomycin, clindamycin, and the macrolides, activity depends on the time of exposure to the drug, at low multiples of the MIC, rather than peak drug concentration. In sinusitis treatment with β-lactam antibiotics (amoxicillin and cephalosporins), time of exposure is critical. In animal infection models, time above MIC has been the only pharmacodynamic parameter to correlate with the clinical efficacy of β-lactam antibiotics.[97] A nationwide surveillance study evaluating 4,489 clinical isolates of *S pneumoniae* for their susceptibility to various antimicrobial agents determined that penicillin susceptibility had a significant impact on time above MIC.[98] Plasma levels of cefprozil, cefaclor, cefixime, cefpodoxime proxetil, and cefuroxime axetil exceeded the geometric mean

TABLE 5. ANTIBIOTICS USED FOR SINUSITIS AND LIKELIHOOD OF EFFECTIVENESS ACCORDING TO PHARMACODYNAMIC AND PHARMACOKINETIC PARAMETERS

Antibiotic	Adult Dosage	Streptococcus pneumoniae			Haemophilus influenzae		Moraxella catarrhalis
		S	I	R	BL−	BL+	
First line							
Amoxicillin (Amoxil, Trimox, Wymox)	250-500 mg tid	+++	++	−	++	−	−
TMP-SMX (Bactrim, Septra)	160 mg/800 mg bid	++	−	−	++	+	+
Second line							
β-Lactams							
Cefpodoxime proxetil (Vantin)	200-400 mg bid	+++	+	−	++	++	+++
Cefprozil (Cefzil)	250-500 mg bid	+++	++	−	++	++	+++
Cefuroxime axetil (Ceftin)	250-500 mg bid	+++	++	−	++	++	+++
Cefdinir (Omnicef)	300 mg bid	+++	+	−	+++	+++	+++
Amoxicillin-clavulanate (Augmentin)	250-500 mg tid*	+++	+	−	+++	+++	+++
	500-875 mg/kg bid*						
Third line							
Macrolide							
Azithromycin (Zithromax)	250 mg qd	+++	±	−	++	+	++
Clarithromycin (Biaxin)	500 mg bid	+++	±	−	++	±	+
Fluoroquinolone							
Ciprofloxacin (Cipro)	500-700 mg bid	++	±	−	+++	+++	+++
Levofloxacin (Levaquin)	500 mg qd	+++	+++	+++	+++	+++	+++
Gatifloxacin (Tequin)	400 mg qd	+++	+++	+++	+++	+++	+++
Moxifloxacin (Avelox)	400 mg qd	+++	+++	+++	+++	+++	+++
Other							
Clindamycin (Cleocin)	150-450 mg tid or qid	+++	++	++	−	−	−

S — penicillin-sensitive, I — intermediate resistance to penicillin, R — penicillin-resistant, BL− — β-lactamase–negative, BL+ — β-lactamase–positive, tid — 3 times daily, bid — twice daily, qd — once daily, qid — 4 times daily, +++ — excellent coverage, ++ — good coverage, + — fair coverage, ± — minimal coverage or efficacy, − — no significant activity, TMP-SMX — trimethoprim-sulfamethoxazole.

*Based on amoxicillin component.

MIC for penicillin-susceptible *S pneumoniae* during 40% of the dosing interval. However, with intermediately penicillin-resistant strains, only cefprozil, cefuroxime axetil, and cefpodoxime proxetil achieved similar concentrations for a similar duration — a finding that suggests that these 3 cephalosporins provide the most reliable pharmacodynamic profiles against penicillin-susceptible and intermediately penicillin-resistant strains.

Other factors to consider include the rate of bactericidal activity, enhancement by increasing drug concentration, and persistent effects, which include postantibiotic effects, postantibiotic sub-MIC effects, and postantibiotic leukocyte enhancement. In vitro measurements may be significantly different from the in vivo response. Focusing only on laboratory pharmacokinetic data discounts the synergistic effect afforded by the actions of host defense mechanisms and bacterial load reduction by the antibiotic.

Table 5 illustrates the antibiotics used in the empiric treatment of acute sinusitis and their effectiveness against *S pneumoniae*, *H influenzae*, and *M catarrhalis*. Penicillin, erythromycin, cephalexin, tetracycline, and cefixime are not generally recommended for the treatment of sinusitis, because of the inadequacy of their spectrum of activity.

Although the cephalosporins offer broad coverage in treating sinusitis, they have varying activities and must be evaluated on an individual basis. The first-generation agents have poor *H influenzae* coverage. Cefaclor, a second-generation agent, has better coverage, but resistance in *H influenzae*, *M catarrhalis*, and *S pneumoniae* is a growing problem. In addition, 3-times-daily dosing is often required, which can affect compliance, and there is a risk of serum sickness–like reactions with cefaclor.[99] Cefadroxil has poor activity against certain gram-negative bacteria and *S pneumoniae*. The use of antibiotics with suboptimal activity has the potential to hasten the emergence of resistant bacteria and is highly discouraged.[4]

Several second- and third-generation cephalosporins that have excellent activity against all major pathogens include cefprozil, cefuroxime axetil, and cefpodoxime proxetil. All are effective in twice-daily dosage and provide adequate coverage of β-lactamase–producing organisms. These 3 cephalosporins are listed in Tables 5 and 6 because they maintain rela-

TABLE 6. FEATURES OF ANTIBIOTICS TO CONSIDER IN SELECTION OF ANTIMICROBIAL AGENTS FOR ACUTE SINUSITIS

Antibiotic	Advantages	Disadvantages
Amoxicillin	Inexpensive Good tolerance Extensive clinical experience	Not effective against β-lactamase–producing organisms Possible activity against normal flora
Amoxicillin-clavulanate	Effective against β-lactamase–producing organisms Twice-daily dosing Active against aerobic and anaerobic respiratory pathogens	Higher rate of cramping and diarrhea No added benefit over amoxicillin alone when treating infections caused by penicillin-resistant strains of *S pneumoniae* Possible activity against normal flora
Trimethoprim-sulfamethoxazole	Used for penicillin-allergic patients Some activity against *H influenzae* Twice-daily dosing Inexpensive Particularly effective against gram-negative organisms	Resistance by group A *Streptococcus* Variably effective against *H influenzae* and *S pneumoniae* Can cause blood dyscrasias, sulfa hypersensitivity, and rashes
Cefuroxime axetil	Good spectrum of activity Twice-daily dosing	Can cause diarrhea and nausea Suspension formulation has bitter taste High relative rate of *C difficile* Expensive
Cefdinir	Good spectrum of activity Once-daily dosing	Activity against penicillin-intermediate and penicillin-resistant strains of *S pneumoniae* not well studied Higher rate of diarrhea
Cefpodoxime proxetil	Spectrum of activity Twice-daily dosing	Higher rate of *C difficile* Higher rate of diarrhea, nausea, vomiting, abdominal pain Metallic aftertaste
Cefprozil	Good spectrum of activity Twice-daily dosing Good-tasting oral suspension Low incidence of side effects	Not as high in vitro activity against β-lactamase–producing strains of *H influenzae*
Azithromycin	Once-daily dosing Alternative for penicillin-sensitive patients Long half-life allows shortened course of therapy	30%-60% of *S pneumoniae* and *H influenzae* strains resistant or not eradicated
Clarithromycin	Twice-daily dosing Alternative for penicillin-sensitive patients Fewer gastrointestinal adverse effects compared to erythromycin	Interacts with theophylline, terfenadine, and astemizole Marginal activity against *H influenzae* Metallic aftertaste
Ciprofloxacin	Broad coverage of gram-negative and atypical organisms	Marginal activity against *S pneumoniae* Higher rates of diarrhea, nausea, headache Safety not established in children younger than 18 years of age Poor gram-positive coverage
Levofloxacin	Once-daily dosing Broad coverage of gram-negative, gram-positive, penicillin-resistant *S pneumoniae*, and atypical organisms	Broad spectrum of activity Not indicated in children
Moxifloxacin	Once-daily dosing Improved gram-positive coverage over older quinolones, especially against *S pneumoniae* and atypical organisms	Broad spectrum of activity Not indicated in children
Gatifloxacin	Once-daily dosing Improved gram-positive coverage over older quinolones, especially against *S pneumoniae* and atypical organisms	Broad spectrum of activity Not indicated in patients younger than 18 years of age
Clindamycin	Good activity against penicillin-resistant *S pneumoniae* and anaerobic bacteria	Higher rate of diarrhea, gastrointestinal upset Can increase risk of *C difficile* infection Not active against gram-negative aerobic bacteria

TABLE 7. FREQUENCY OF POSITIVE TESTS FOR
CLOSTRIDIUM DIFFICILE DIARRHEA

Antibiotic	No. of Risk Periods*	Positive Test No.	%
Amoxicillin	39	7	17.9
Cefixime	9	5	55.6
Cefaclor	4		
Cefuroxime	22	9	40.9
Cefprozil	8		
Cephalexin	16	9	56.3
Ciprofloxacin	15	1	6.7
Clarithromycin	2		
Amoxicillin-clavulanate	25	9	36.0
Clindamycin	1		
Erythromycin-sulfisoxazole	2		
Trimethoprim-sulfamethoxazole	20	2	10.0

*Risk periods for which *Clostridium difficile* tests were performed. Data from Levy et al.[101]

tively high levels of activity against intermediate-level resistant pneumococci.[12] Cefpodoxime proxetil has good activity against *H influenzae* and *M catarrhalis*; however, its metallic aftertaste can compromise patient compliance. Cefixime, loracarbef, and ceftibuten are not included on Tables 5 and 6 because of their reduced activity against *S pneumoniae*, which may compromise clinical efficacy.[100] However, cefixime and ceftibuten can be combined with another agent (ie, clindamycin) to cover *S pneumoniae*.

The risk of *Clostridium difficile* diarrhea is another consideration in patients being treated with prolonged courses of antibiotic therapy. Although it is commonly described in association with substantial morbidity in hospitalized patients, it can occur in the ambulatory care setting. The risk of *C difficile* diarrhea was recently evaluated in a retrospective longitudinal study of 4 large managed-care health plans.[101] The analysis identified patients with a claim indicator for a *C difficile* toxin test. A single antibiotic group was identified in 217 enrollees in the analysis (Table 7[101]). Cephalexin and cefixime had the highest frequencies of positive *C difficile* tests, which were 56.3% and 55.6%, respectively. Cephalexin and cefixime showed a statistically significant association with *C difficile* diarrhea, and amoxicillin-clavulanate and cefuroxime showed a trend toward an increased risk for *C difficile* diarrhea. In this study, antibiotics that demonstrated minimal association with positive *C difficile* tests included cefaclor, cefadroxil, and cefprozil.

Antibiotic resistance may be caused by a variety of mechanisms (eg, enzymatic degradation or altered antibiotic binding sites). β-Lactamase–producing organisms cause enzymatic degradation of antibiotics with a β-lactam moiety in their chemical structure. Clavulanate is a β-lactamase inhibitor; therefore, amoxicillin-clavulanate is effective against β-lactamase–producing organisms (eg, β-lactamase–producing strains of *H influenzae* and *M catarrhalis*).

The mechanism of *S pneumoniae* resistance is different from that of β-lactamase production. *Streptococcus pneumoniae* resistance occurs because of an altered penicillin binding site. Amoxicillin-clavulanate offers no advantage over amoxicillin alone in the treatment of infections caused by resistant strains of *S pneumoniae*.

As previously discussed, higher routine doses of amoxicillin may be needed in certain circumstances. A common recommendation is to double the usual dose. With currently available formulations of amoxicillin-clavulanate, 2 prescriptions are required (1 for amoxicillin and the other for amoxicillin-clavulanate) to achieve a higher dose of amoxicillin without increasing the dose of clavulanate, a gastrointestinal mucosal irritant. The complexity of such a regimen may compromise patient compliance.

The newer macrolides (clarithromycin and azithromycin) may be acceptable second-line agents, specifically in patients who are allergic to penicillin. Resistance among the pneumococci to these agents is increasing.[50,96] Breakpoints for resistance by the NCCLS are ≥1 µg/mL for erythromycin and clarithromycin and ≥2 µg/mL for azithromycin, although the NCCLS recommends that erythromycin antimicrobial susceptibility test results can predict the activities of other macrolides. Erythromycin-resistant strains are resistant to clarithromycin, azithromycin, and usually penicillin.[102] *Haemophilus influenzae*, which is susceptible in vitro to azithromycin, may survive in an infected fluid because of lower extracellular concentration of the antibiotic.[103] The mechanisms of action of macrolide resistance may be enzymatic deactivation or active efflux of the antibiotic across the bacterial cell membrane or ribosomal alterations.[104,105] Clindamycin can be used for infections caused by *S pneumoniae*, but it does not eradicate *H influenzae* or *M catarrhalis* and is consequently inappropriate empirical therapy for sinusitis.

The newer fluoroquinolones — levofloxacin, moxifloxacin, and gatifloxacin — have good in vitro activity against *S pneumoniae*, including penicillin-resistant isolates, and excellent tissue penetration into the sinuses. The first-line use of the fluoroquinolones should be restricted to patients with moderate-to-severe infections or recent antibiotic failures. There are differences between the in vitro activities of the different fluoroquinolones against *S pneumoniae*.[106,107]

Gatifloxacin and moxifloxacin have greater in vitro activity than levofloxacin when tested against *S pneumoniae*. The newer fluoroquinolones offer once-daily dosing and have low phototoxic potential.[108-110] Currently, the fluoroquinolone antibiotics are not indicated for patients younger than 18 years of age. The role of these agents has not been clearly established in the treatment of acute sinusitis. Emerging reports of fluoroquinolone resistance among pneumococci underscore the need to curtail the inappropriate use of these drugs for infections that can be treated with β-lactam or macrolide antibiotics.[106]

The Joint Task Force on Practice Parameters for Allergy and Immunology has developed guidelines to aid the clinician in therapeutic decision-making.[111] This comprehensive document covers every major aspect of sinusitis in various formats, and it is the basis for the treatment algorithms for selecting antimicrobial therapy (Figs 4 and 5). Sinusitis can be classified as acute (<4 weeks), subacute (4 to 12 weeks), or chronic (>12 weeks). Antibiotic therapy should be considered for acute sinusitis if the acute illness has persisted for more than 7 days, or less than 7 days in patients with fever and headaches who are not responsive to analgesic management, and for subacute sinusitis cases. An initial otolaryngological consultation is recommended for chronic sinusitis.

The initial choice of antibiotic should begin with amoxicillin or TMP-SMX and consider cost, bacterial resistance patterns in the locality, the severity and duration of infection, and risk factors prompting consideration of a second-line agent. The choice of a second-line antibiotic also should include proven efficacy, an allergic history, the previous response to the selected antibiotic, and the physician's experience. In all cases, the selection of an antibiotic should be tempered by patient-focused considerations.

DURATION OF THERAPY

The symptoms should abate within a few days after the initiation of treatment, and 10 to 14 days is considered an adequate treatment interval. A longer treatment interval may be warranted if symptoms persist. Researchers have looked at shorter courses of antimicrobial treatment to lower costs, reduce side effects, increase compliance, reduce the potential for resistance, and decrease the impact on commensal flora.[112] Although the results of these studies are promising, further studies of short-course therapy are needed, especially in children, and clinical judgment is paramount.

The majority of patients with sinusitis are treated on an outpatient basis that necessitates appropriate follow-up to assess compliance.[113] Follow-up times vary widely according to the patient's age, risk factors, and history.[114] Additional evaluations are necessary if symptoms persist or worsen, perhaps because of resistant bacteria or poor antimicrobial coverage. Children should be considered at greater risk for recurrence if they are younger than 6 months of age, attend day care, live with a smoker, or have a history of multiple URTIs.

Physicians should consider immunologic defects in children who do not respond to treatment. The majority of children who have severe sinusitis have inadequate humoral defenses[115] and prolonged courses of antibiotics. The use of antibiotics in children is controversial. Many cases resolve spontaneously, whereas others tend to progress; antibiotic use should be limited to highly selected patients.[29] Antibiotics should be used in children whose signs and symptoms persist for 10 to 14 days or longer without improvement.[33,82]

ADJUNCTIVE TREATMENTS

Adjunctive treatments are designed to promote ciliary function and decrease edema. Although most are unproved, these measures are not expensive, complicated, or associated with major side effects. Hence, they represent reasonable supportive measures. Saline nasal sprays, humidifiers, warm aerosols, steam, aromatic vapors, hot soups, and teas moisturize the nasal cavity and remove thick mucus crusts and thus help minimize symptoms.

Topical decongestants (eg, phenylephrine hydrochloride, oxymetazoline hydrochloride) relieve nasal congestion by stimulating mucosal α-adrenergic receptors, thereby shrinking the edematous mucosa and relieving obstruction.[116] The use of these sprays should be limited to 3 days to avoid rhinitis medicamentosa, which can worsen nasal congestion. Systemic decongestants (eg, pseudoephedrine, phenylpropanolamine hydrochloride) may reduce nasal congestion, but typically have side effects that include insomnia or hyperactivity. The use of systemic decongestants is not recommended in children, especially when there is a potential for cardiac stimulation, hypertension, or neurologic complications.[13,117,118]

Studies in adults show that when decongestants are prescribed in conjunction with antibiotics, both symptoms and total costs decrease — a finding suggesting that physicians should consider this dual approach to treating sinusitis.[119] The expectorant guaifenesin, 1,200 mg twice daily in adults, can help thin secretions and improve ciliary action, thus lessening mucus stasis and improving drainage.
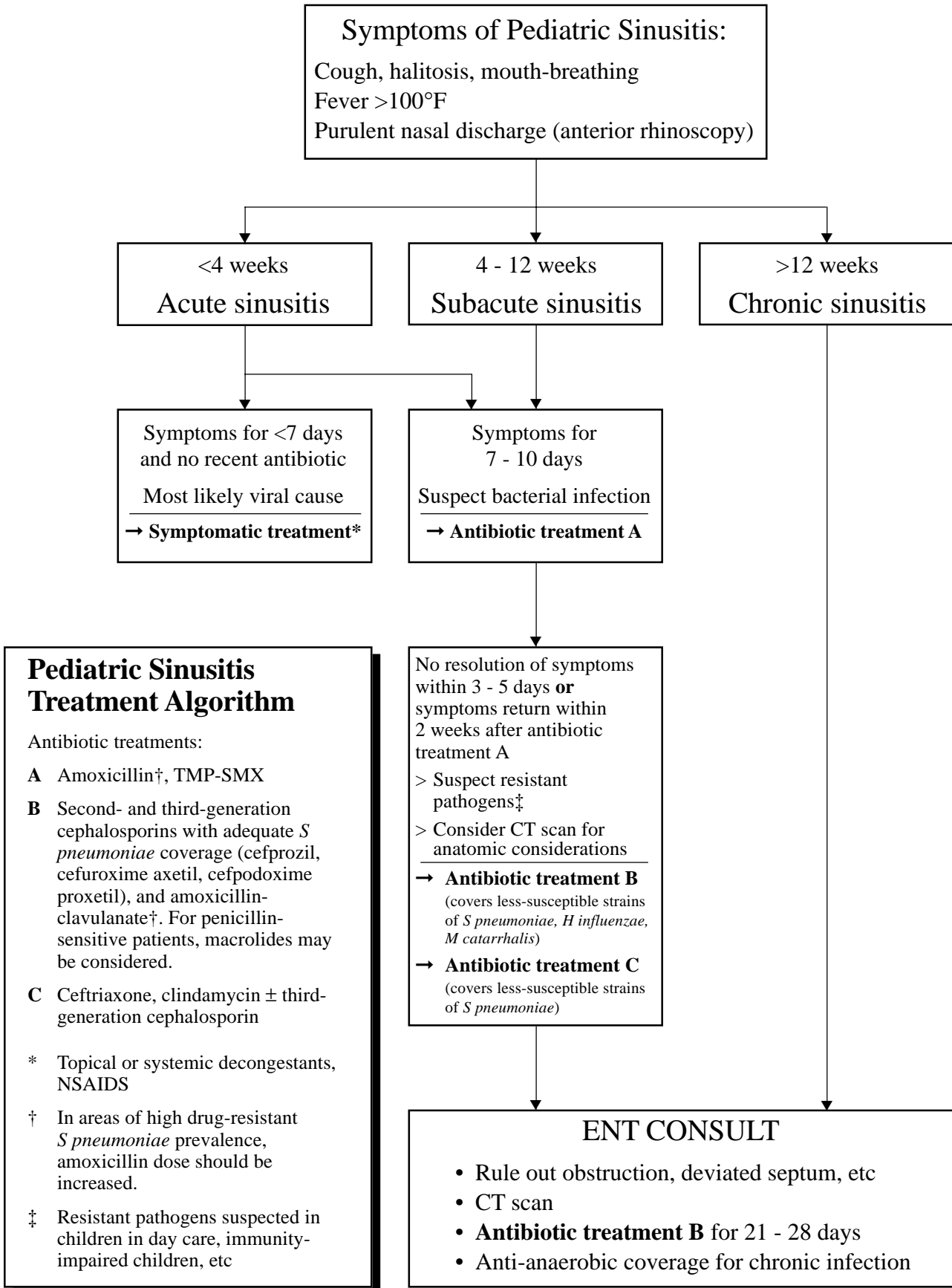
Symptoms of Pediatric Sinusitis:

Cough, halitosis, mouth-breathing
Fever >100°F
Purulent nasal discharge (anterior rhinoscopy)

<4 weeks
Acute sinusitis

4 - 12 weeks
Subacute sinusitis

>12 weeks
Chronic sinusitis

Symptoms for <7 days
and no recent antibiotic

Most likely viral cause

→ **Symptomatic treatment***

Symptoms for
7 - 10 days

Suspect bacterial infection

→ **Antibiotic treatment A**

Pediatric Sinusitis Treatment Algorithm

Antibiotic treatments:

A Amoxicillin†, TMP-SMX

B Second- and third-generation cephalosporins with adequate *S pneumoniae* coverage (cefprozil, cefuroxime axetil, cefpodoxime proxetil), and amoxicillin-clavulanate†. For penicillin-sensitive patients, macrolides may be considered.

C Ceftriaxone, clindamycin ± third-generation cephalosporin

* Topical or systemic decongestants, NSAIDS

† In areas of high drug-resistant *S pneumoniae* prevalence, amoxicillin dose should be increased.

‡ Resistant pathogens suspected in children in day care, immunity-impaired children, etc

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No resolution of symptoms within 3 - 5 days **or** symptoms return within 2 weeks after antibiotic treatment A

> Suspect resistant pathogens‡

> Consider CT scan for anatomic considerations

→ **Antibiotic treatment B**
(covers less-susceptible strains of *S pneumoniae, H influenzae, M catarrhalis*)

→ **Antibiotic treatment C**
(covers less-susceptible strains of *S pneumoniae*)

ENT CONSULT

• Rule out obstruction, deviated septum, etc
• CT scan
• **Antibiotic treatment B** for 21 - 28 days
• Anti-anaerobic coverage for chronic infection

Fig 4. Algorithm for selecting antimicrobial therapy for acute sinusitis in children.

Symptoms of Adult Sinusitis:

Frontal headache (NSAID nonresponsive)
Tooth pain, fever >100°F
Purulent nasal discharge (anterior rhinoscopy)

<4 weeks — Acute sinusitis

4 - 12 weeks — Subacute sinusitis

>12 weeks — Chronic sinusitis

Symptoms for <7 days and no recent antibiotic

Most likely viral cause

→ **Symptomatic treatment***

Symptoms for 7 - 10 days

Suspect bacterial infection

→ **Antibiotic treatment A**

No resolution of symptoms within 3 - 5 days **or** symptoms return within 2 weeks after antibiotic treatment A

> Suspect resistant pathogens‡

> Consider CT scan for anatomic considerations

→ **Antibiotic treatment B**
(covers less-susceptible strains of *S pneumoniae, H influenzae, M catarrhalis*)

→ **Antibiotic treatment C**
(covers less-susceptible strains of *S pneumoniae*, β-lactamase–producing *H influenzae*)

Adult Sinusitis Treatment Algorithm

Antibiotic treatments:

A Amoxicillin†, TMP-SMX

B Second- and third-generation cephalosporins with adequate *S pneumoniae* coverage (cefprozil, cefuroxime axetil, cefpodoxime proxetil), and amoxicillin-clavulanate†

C Fluoroquinolones with adequate *S pneumoniae* coverage (gatifloxacin, moxifloxacin, levofloxacin); clindamycin ± third-generation cephalosporin

* Topical or systemic decongestants, NSAIDS

† In areas of high drug-resistant *S pneumoniae* prevalence, amoxicillin dose should be increased.

‡ Resistant pathogens suspected in high-risk patients, such as patients previously treated with antibiotics, parents of children in day care, immune-impaired patients, patients with severe allergies, etc

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ENT CONSULT

- Rule out obstruction, deviated septum, etc
- CT scan
- **Antibiotic treatment B** or **C** for 21 - 28 days
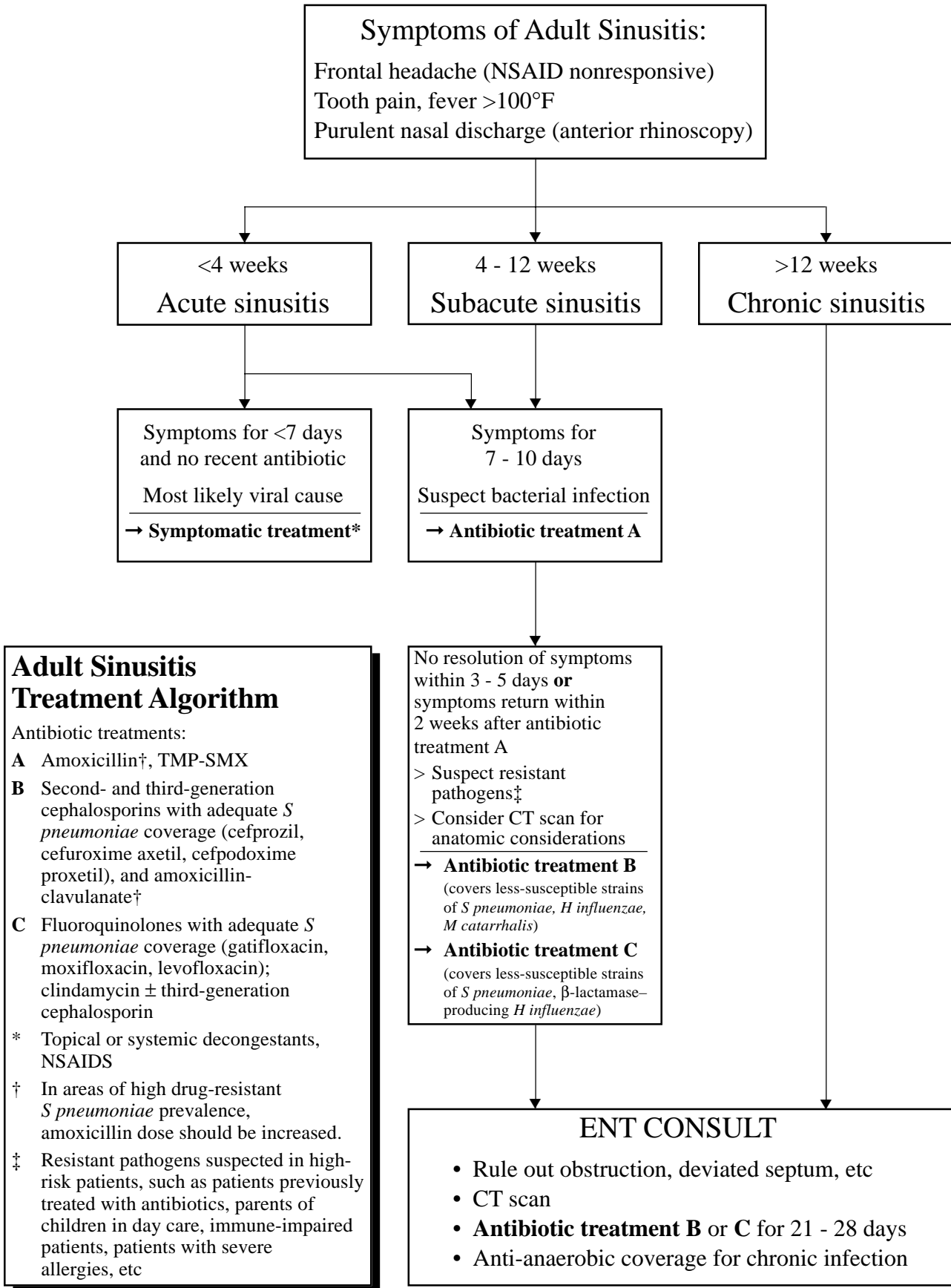- Anti-anaerobic coverage for chronic infection

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Fig 5. Algorithm for selecting antimicrobial therapy for acute sinusitis in adults.

TABLE 8. ANTIMICROBIAL REGIMENS FOR ACUTE SINUSITIS

Antimicrobial Agent	Dose and Duration	Average Wholesale Price Regimen Cost*
Amoxicillin (generic)†	500 mg q12h for 14 d	$8.73
	875 mg q12h for 14 d	$27.13
Amoxicillin-clavulanate (Augmentin)	500 mg/125 mg q8h for 10 d	$106.88
	875 mg/125 mg q12h for 10 d	$95.15
Cefprozil (Cefzil)	250 mg q12h for 10 d	$65.94
	500 mg q12h for 10 d	$130.76
Cefuroxime axetil (Ceftin)	250 mg q12h for 10 d	$81.55
Cefaclor (Ceclor)†	500 mg q12h for 10 d	$77.89
Loracarbef (Lorabid)	400 mg q12h for 10 d	$100.00
Cefixime (Suprax)†	200 mg q12h for 10 d	$74.99
Cefdinir (Omnicef)	300 mg q12h for 10 d or	$70.56
	600 mg q24h for 10 d	$141.12
Trimethoprim-sulfamethoxazole (generic)†	160 mg/800 mg q12h for 10 d	$8.02
Azithromycin (Zithromax)†	500 mg on day 1 and	$40.53
	250 mg on days 2-5 or	
	500 mg for 3 days	
Clarithromycin (Biaxin)	500 mg q12h for 14 d	$91.28
Levofloxacin (Levaquin)‡	500 mg q24h for 10 d	$85.34
	500 mg q24h for 14 d	$119.48
Moxifloxacin (Avelox)‡	400 mg q24h for 10 d	$87.12
Gatifloxacin (Tequin)‡	400 mg q24 for 10 d	$70.25

*1999 Redbook. Montvale, NJ: Medical Economics Company, 2000;19(2):15-64.

†**Not approved in United States for treatment of sinusitis.**

‡Not commonly used to treat community-acquired acute bacterial sinusitis, but may have important role for highly resistant or multidrug-resistant strains.

Antihistamines should not be used routinely in acute bacterial sinusitis. They may dry nasal and sinus secretions and thereby limit mucus clearance from the sinus cavity. Antihistaminic therapy should be considered when there are signs and symptoms that suggest an allergic history. Nasal steroids theoretically alter the inflammatory response in rhinosinusitis and decrease edema and obstruction. These agents are not unequivocally effective and are therefore not routinely recommended in the treatment of acute sinusitis, although they may have some benefits in chronic disease.

ECONOMIC BURDEN

Sinusitis exerts a substantial economic burden on society. It is a serious, debilitating, and costly disease. Sinusitis is associated with high direct health care system costs, including facility usage, professional fees, laboratory and clinical testing costs, medication, surgical costs, socioeconomic costs, and reduced quality of life. In a recent 1-year study, 26.7 million patient visits were attributed to sinusitis and related airway disorders, at a cost of $5.78 billion.[6] Cases in children accounted for 30.6% of the overall costs ($1.77 billion), and adults accounted for 69.4% of the overall costs ($4 billion).

The increasing frequency of penicillin-resistant *S*

pneumoniae may increase the rate of treatment failures, greatly increasing treatment costs.[120] Costs of treating sinusitis are also rising because of the increasing prevalence of β-lactamase–producing bacteria. Often, costs are underestimated because indirect and out-of-pocket expenses are not considered (ie, over-the-counter adjunctive treatments). Each year, it is estimated that adults have 12.5 million lost workdays, 58.7 million days of restricted activity, and 20.3 million bed-days because of sinusitis.[6]

Patients who have recurring disease use more health care resources and increase costs. Ober[119] showed a positive correlation between the number of episodes and costs in treating sinusitis. Costs increased from $304 for the first episode to $667 for the second episode to $1,743 for the third episode. Unfortunately, as the number of episodes increased, the choice of antibiotics did not change from amoxicillin. A similar pattern of represcribing amoxicillin after an initial acute otitis media episode was observed.[120] Episode-to-episode pattern changes indicated that amoxicillin was prescribed in 67% of initial cases, 47% of second visits, and 39% of third visits.

The judicious use of a more appropriate second-generation cephalosporin is likely to decrease costs in patients with multiple episodes of sinusitis. The US and Canadian guidelines recommend the use of sec-

ond-line agents to treat recurring infections.[51] Physicians must consider that less-expensive agents that fail may contribute to the emergence of resistance.

Antibiotic costs represent a small portion (10% to 16%) of the total costs of sinusitis treatment, but the inappropriate selection of antibiotic therapy can significantly increase aggregate health care costs (Table 8).[119] Physicians must determine how families will pay for prescriptions in order to remove barriers that may prevent them from obtaining a drug.[114] Out-of-pocket costs may be a significant barrier to compliance. For children, physicians should consider the amount of antibiotic prescribed versus the weight of the patient. This prevents waste and the potential of using leftover antibiotics for future episodes.[114] Although the cost of second-line antibiotics may be more than that of amoxicillin, the overall cost of failure may outweigh the medication cost. The larger per-episode costs, including revisits, additional clinical and laboratory testing, and professional and emergency room fees, must be considered.

Selecting antimicrobials that are clinically and bacteriologically effective, associated with good compliance, and well tolerated optimizes economic benefit.[121] The palatability of an antimicrobial may be the deciding factor in choice when comparable efficacy exists. Double-blind taste comparisons of pediatric antibiotic suspensions found that the cephalosporins tend to be preferred. Loracarbef, cefadroxil, cefprozil, and cefixime were the 4 highest-ranked antibiotics.[122]

WHEN TO REFER

Improperly treated sinus infections may spread to nearby structures (eye, dura, or venous drainage) through anastomosing veins or by direct extension.[12] Sinusitis is the primary source of infection in two thirds of patients with intracranial abscesses and in 5% of community-acquired bacterial meningitis cases.[12] A patient should be referred to a specialist when a potentially serious complication arises. A referral to an otolaryngologist or an allergist is appropriate when there are recurrent or chronic symptoms, nasal polyposis, asthma, or allergies. Otolaryngologists serve a primary role in the management of complicated and chronic sinusitis.[123] The complications that require a referral to an otolaryngologist include a deteriorating patient condition, treatment failure, immunocompromise, or the development of a nosocomial infection.[80]

Although CT scanning and magnetic resonance imaging have a minor role in the diagnosis of acute bacterial sinusitis, they have a definite role in the management of complicated sinusitis.[94] A CT scan is required to diagnose chronic sinusitis. Computed tomographic scans are superior to plain radiographs in the delineation of sinus abnormalities and have greater sensitivity and specificity.[30,124] In children, CT scanning confirms the most common site of infection to be the ethmoid infundibulum and the anterior ethmoid complex.[125] However, CT scans should be reserved for children with complicated sinus disease, numerous recurrences, or protracted or unresponsive cases in which surgery is contemplated.

A child should be referred for cultures when he or she is severely ill or toxic-appearing, when symptoms progress despite medical management, when he or she is immunocompromised, or when suppurative complications are present.[8] A skilled otolaryngologist should perform the aspiration of the maxillary sinuses. Recovery of bacteria at a density of 10^4 colony-forming units per milliliter represents true infection.[126,127] In addition to the 3 most common pathogens, *S aureus* and anaerobes may be present. Intravenous antibiotics are recommended in severely ill children.

Patients with acute sinusitis rarely require surgical intervention or sinus aspiration to ventilate a sinus that is unresponsive to antimicrobial treatment.[33] Surgery should be considered only when all medical options have been exhausted, and it is generally reserved for patients with refractory disease or anatomic abnormalities. Evaluations by a medical specialist and a surgical specialist may be warranted because of the high complication rate of surgery. Surgery in children may interfere with the development of the face, possibly leading to asymmetrical development.[125] The role of adenotonsillectomy in treating pediatric sinusitis is unclear. Consultation with an otolaryngologist helps determine the size of the tonsils and adenoids, their role in possible sinus obstruction, and the need for their removal.[128]

A referral to an allergist is appropriate when the patient has a significant allergic history. Medical and surgical treatment of sinusitis in patients with asthma reduces the use of asthma medications. This type of referral may be necessary even without complications.[129]

CONCLUSIONS

The literature is full of clinical studies and review articles that deal with sinusitis. Unfortunately, there are few universally accepted guidelines for diagnosis and management. In 1997, the Canadian Sinusitis Symposium developed guidelines for the diagnosis and treatment of sinusitis.[51] Rachelefsky[130] discussed the need for practical national guidelines for the diagnosis and treatment of rhinitis, but there is only minimal mention of sinusitis. The Joint Task

Force on Practice Parameters for Allergy and Immunology has developed guidelines to aid the clinician in decision-making.[111] This comprehensive document covers every major aspect of sinusitis in various formats (Figs 4 and 5).

The optimal management of acute sinusitis is controversial.[6] Primary care physicians must focus on better diagnosis of this condition. A proper diagnosis that focuses on differentiation between viral disease and bacterial infection is required to offer appropriate treatment. This diagnosis can rely largely on patient history and physical examination. Rarely are laboratory tests required. Treatment for sinusitis should focus on relieving the obstruction, treating the infection, thinning the mucus, and opening the sinus ostia.

When a bacterial origin is suspected, an antibiotic should be selected on the basis of resistance patterns found in the community. Regardless of patient pressure, prescribing antibiotics for nonbacterial causes is to be discouraged and replaced with patient education and attention. Appropriate antibiotic selection and duration of use is important to achieve efficacy and prevent antibiotic resistance. Adjunctive treatment may aid in the resolution of signs and symptoms. Patients who do not respond to treatment should be referred to an otolaryngologist to minimize complications. Appreciation of the high incidence of sinusitis and its impact on quality of life should stimulate primary care physicians to properly recognize the subtle clinical presentation of acute bacterial sinusitis and offer appropriate aggressive treatment.

REFERENCES

1. United States Department of Health and Human Services. National health survey. Prevalence of selected chronic conditions, United States, 1983–85. Hyattsville, Md: US Department of Health and Human Services, 1987.

2. Adelglass J, Jones TM, Ruoff G, Kahn J, Wiesinger B, Reilly-Gauvin K, et al. A multicenter, investigator-blinded, randomized comparison of oral levofloxacin and oral clarithromycin in the treatment of acute bacterial sinusitis. Pharmacotherapy 1998;18:1255-63.

3. Gooch WM III. Antibacterial management of acute and chronic sinusitis. Managed Care Interface 1999(February):92-4.

4. Kaliner MA, Osguthorpe JD, Fireman P, Anon J, Georgitis J, Davis M, et al. Sinusitis: bench to bedside. Current findings, future directions. J Allergy Clin Immunol 1997;99(suppl): S829-S848.

5. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. Otolaryngol Head Neck Surg 1995;113:104-9.

6. Ray NF, Baraniuk JN, Thamer M, Rinehart C, Gergen P, Kaliner M, et al. Healthcare expenditures for sinusitis in 1996. Contributions of asthma, rhinitis, and other airway disorders. J Allergy Clin Immunol 1999;103:408-14.

7. Conde MV, Williams JW, Witsell DL, Piccirillo JF. Management of a 35-year-old man with acute nasal and sinus complaints. JCOM 1998;5:63-76.

8. Lusk RP, Stankiewicz JA. Pediatric rhinosinusitis. In: Anon JB, ed. Report of the Rhinosinusitis Task Force Committee Meeting. Otolaryngol Head Neck Surg 1997;117(suppl):S53-S57.

9. Wald ER. Expanded role of group A streptococci in children with upper respiratory infections. Pediatr Infect Dis J 1999; 18:663-5.

10. Wald ER. Microbiology of acute and chronic sinusitis in children and adults. Am J Med Sci 1998;316:13-20.

11. Fagnan LJ. Acute sinusitis: a cost-effective approach to diagnosis and treatment. Am Fam Physician 1998;58:1795-802, 805-6.

12. Poole MD. A focus on acute sinusitis in adults: changes in disease management. Am J Med 1999;106(5A):38S-47S.

13. Zacharisen MC, Kelly KJ. Allergic and infectious pediatric sinusitis. Pediatr Ann 1998;27:759-66.

14. Simon MW. Treatment of acute sinusitis in childhood with ceftibuten. Clin Pediatr 1999;38:269-72.

15. Jones NS. Current concepts in the management of paediatric rhinosinusitis. J Laryngol Otol 1999;113:1-9.

16. Laurier C, Lachaine J, Ducharme M. Economic evaluation of antibacterials in the treatment of acute sinusitis. Pharmacoeconomics 1999;15:97-113.

17. National Center for Health Statistics. Vital and health statistics: current estimates from National Health Interview Survey No. 190. Washington, DC: US Department of Health and Human Services, 1994.

18. Benson V, Marano MA. Current estimates from the National Health Interview Survey, 1992. Vital Health Stat 1994; 189:1-269.

19. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. JAMA 1995;273:214-9.

20. Mainous AG III, Hueston WJ, Clark JR. Antibiotics and upper respiratory infection: do some folks think there is a cure for the common cold? J Fam Pract 1996;42:357-61.

21. Hamm RM, Hicks RJ, Bemben DA. Antibiotics and respiratory infections: are patients more satisfied when expectations are met? J Fam Pract 1996;43:56-62.

22. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. JAMA 1997;278:901-4.

23. Wang EEL, Einarson TR, Kelner JD, Conly JM. Antibiotic prescribing for Canadian preschool children: evidence of overprescribing for viral respiratory infections. Clin Infect Dis 1999;29:155-60.

24. Schwartz B, Mainous AG, Marey SM. Why do physicians prescribe antibiotics for children with upper respiratory tract infections? JAMA 1998;279:881-2.

25. Chen RF. Antibiotics for children with upper respiratory tract infections [Letter]. JAMA 1998;280:1399.

26. Woolf SH. Antibiotics for children with upper respiratory tract infections [Letter]. JAMA 1998;280:1400.

27. Ober NS. Antibiotics for adult respiratory infections: clinical considerations and management pitfalls. Drug Benefit

Trends 1998;10:10-6.

28. Ober NS. Developing a definition for appropriate antibiotic therapy — patient-, disease-, and drug-related factors. Drug Benefit Trends 1998;10:17-22.

29. O'Brien KL, Dowell SF, Schwartz B, Marcy SM, Phillips WR, Gerber MA. Acute sinusitis: principles of judicious use of antimicrobial agents. Pediatrics 1998;101(suppl 1):174-7.

30. Clement PAR, Bluestone CD, Gordts F, Lusk R, Otten F, Goossens H, et al. Management of rhinosinusitis in children. Consensus Meeting, Brussels, Belgium, September 13, 1996. Arch Otolaryngol Head Neck Surg 1998;124:31-4.

31. Fireman P. Diagnosis of sinusitis in children. Emphasis on the history and physical examination. J Allergy Clin Immunol 1992;90:433-6.

32. Wald ER. Sinusitis in children. N Engl J Med 1992;326:319-23.

33. Wald ER. Sinusitis. Pediatr Ann 1998;27:811-8.

34. Wald ER, Dashefsky B, Guerra N, Byers C. Frequency and severity of infections in day care. J Pediatr 1988;112:540-6.

35. Wald ER, Guerra N, Byers C. Frequency and severity of infections in day care: three-year follow-up. J Pediatr 1991;118:509-14.

36. Willner A, Choi SS, Vexina LG, Lazar RH. Intranasal anatomic variations in pediatric sinusitis. Am J Rhinol 1997;11:355-60.

37. Ahuja GS, Thompson J. What role for antibiotics in otitis media and sinusitis? Postgrad Med 1998;104:93-9, 103-4.

38. Brook I. Bacteriologic features of chronic sinusitis in children. JAMA 1981;246:967-9.

39. Otten FWA, Grote JJ. Treatment of chronic maxillary sinusitis in children. Int J Pediatr Otorhinolaryngol 1988;15:269-78.

40. Tinkleman DG, Silk HJ. Clinical and bacteriologic features of chronic sinusitis in children. Am J Dis Child 1989;143:938-41.

41. Otten HW, Antvelink JB, Ruyter De Wildt H, Rietema SJ, Siemelink RJG, Hordijk GJ. Is antibiotic treatment of chronic sinusitis effective in children? Clin Otolaryngol 1994;19:215-7.

42. Shapiro NL, Pransky SM, Hartin M, Bradley JS. Documentation of the prevalence of penicillin-resistant *Streptococcus pneumoniae* isolated from the middle ear and sinus fluid of children undergoing tympanocentesis or sinus lavage. Ann Otol Rhinol Laryngol 1999;108:629-33.

43. Applebaum PC. Antimicrobial resistance in *Streptococcus pneumoniae*: an overview. Clin Infect Dis 1992;15:77-83.

44. Jorgensen JH, Doern GV, Maher LA, Howell AW, Redding JS. Antimicrobial resistance among respiratory isolates of *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pneumoniae* in the United States. Antimicrob Agents Chemother 1990;34:2075-80.

45. Thornsberry C, Brown SD, Yee YC, Bouchillon S, Marler J, Rich T. Increasing penicillin resistance in *Streptococcus pneumoniae* in the US: effect on susceptibility to oral cephalosporins. Infect Med 1993;10(suppl):15-24.

46. Pikis A, Akram S, Donkersloot JA, Campos JM, Rodriguez WJ. Penicillin-resistant pneumococci from pediatric patients in the Washington, DC, area. Arch Pediatr Adolesc Med 1995;149:30-5.

47. Doern GV, Brueggemann AB, Holley HP Jr, Rauch AM. Antimicrobial resistance of *Streptococcus pneumoniae* recovered from outpatients in the United States during winter months of 1994 to 1995: results of a 30-center national surveillance study. Antimicrob Agents Chemother 1996;40:1208-13.

48. Cram DL Jr, Moore K, Adler K, Alles E, Lian J, Bannister K. California *Streptococcus pneumoniae* resistance project (CASPr): the extent and impact of resistance in a Medi-Cal population. California Pharmacist 1996(Winter):34-50.

49. Thornsberry C. Activity of selected antimicrobials against penicillin-resistant *S pneumoniae* isolates. Infect Med 1997;14 (suppl A):13-9.

50. Thornsberry C, Ogilvie P, Kahn J, Mauriz Y, and the Laboratory Investigator Group. Surveillance of antimicrobial resistance in *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* in the United States in 1996-1997 respiratory season. Diagn Microbiol Infect Dis 1997;29:249-57.

51. Low DE, Desrosiers M, McSherry J, Garber G, Williams J Jr, Remy H, et al. A practical guide for the diagnosis and treatment of acute sinusitis. Can Med Assoc J 1997;156(suppl 6):S1-S14.

52. Wallace RJ Jr, Steingrube VA, Nash DR, Hollis DG, Flanagan C, Brown BA, et al. BRO beta-lactamases of *Branhamella catarrhalis* and *Moraxella* subgenus Moraxella, including evidence for chromosomal beta-lactamase transfer by conjugation in *B catarrhalis*, *M nonliquefaciens*, and *M lacunata*. Antimicrob Agents Chemother 1989;33:1845-54.

53. Doern GV, Brueggemann AB, Pierce G. Prevalence of antimicrobial resistance among 723 outpatient clinical isolates of *Moraxella catarrhalis* in the United States in 1994 and 1995: results of a 30-center national surveillance survey. Antimicrob Agents Chemother 1996;40:2884-6.

54. Doyle MG, Morrow AL, Van R, Pickering LK. Intermediate resistance of *Streptococcus pneumoniae* to penicillin in children in day-care centers. Pediatr Infect Dis J 1992;11:831-5.

55. Mainous AG III, Evans ME, Hueston WJ, Titlow WB, McCown LJ. Patterns of antibiotic-resistant *Streptococcus pneumoniae* in children in a day-care setting. J Fam Pract 1998;46:142-6.

56. Arnold KE, Leggiardo RJ, Breiman RF, Lipman HB, Schwartz B, Appleton MA, et al. Risk factors for carriage of drug-resistant *Streptococcus pneumoniae* among children in Memphis, Tennessee. J Pediatr 1996;128:757-64.

57. Duchin JS, Breiman RF, Diamond A, Lipman H, Block S, Hedrick J, et al. High prevalence of multidrug-resistant *Streptococcus pneumoniae* among children in a rural Kentucky community. Pediatr Infect Dis J 1995;14:745-50.

58. Boken DJ, Chartrand SA, Goering RV, Kruger R, Harrison CJ. Colonization with penicillin-resistant *Streptococcus pneumoniae* in a child-care center. Pediatr Infect Dis J 1995;14:879-84.

59. Mason EO Jr, Kaplan SL. Penicillin-resistant pneumococci in the United States [Letter]. Pediatr Infect Dis J 1995;14:1017-8.

60. Surveillance Data, Inc. Bacterial resistance tracking. August 1998/February 1999. Plymouth Meeting, Pa: Surveillance Data, Inc, 1999.

61. Brook I, Gober AE. Monthly changes in the rate of recovery of penicillin-resistant organisms from children. Pediatr Infect Dis J 1997;16:255-7.

62. Brook I. β-lactamase–producing bacteria recovered after clinical failures with various penicillin therapy. Arch Otolaryngol 1984;110:228-31.

63. Brook I, Gober AE. Emergence of beta-lactamase–producing aerobic and anaerobic bacteria in the oropharynx of children following penicillin chemotherapy. Clin Pediatr 1984;23: 338-41.

64. Tunér K, Nord CE. Emergence of beta-lactamase–producing anaerobic bacteria in the tonsils during penicillin treatment. Eur J Microbiol 1986;5:399-404.

65. Sanders CC, Nelson GE, Sanders WE Jr. Bacterial interference. IV. Epidemiological determinants of the antagonist activity of the normal flora against group A streptococci. Infect Immunol 1977;16:599-603.

66. Sprunt K, Redman W. Evidence suggesting importance of role of interbacterial inhibition in maintaining balance of normal flora. Ann Intern Med 1968;68:579-90.

67. Brook I, Gober AE. Bacterial interference in the nasopharynx following antimicrobial therapy of acute otitis media. J Antimicrob Chemother 1998;41:489-92.

68. Brook I. The role of β-lactamase–producing bacteria in the persistence of streptococcal tonsillar infection. Rev Infect Dis 1984;6:601-7.

69. Brook I, Yocum P, Frazier EH. Bacteriology and beta-lactamase activity in acute and chronic maxillary sinusitis. Arch Otolaryngol Head Neck Surg 1996;122:418-22.

70. Holleman DR Jr, Williams JW Jr, Simel DL. Usual care and outcomes in patients with sinus complaints and normal results of sinus roentgenography. Arch Fam Med 1995;4:246-51.

71. Berg O, Carenfelt C. Analysis of symptoms and clinical signs in the maxillary sinus empyema. Acta Otolaryngol 1988; 105:343-9.

72. Lanza DC, Kennedy DW. Adult rhinosinusitis defined. In: Anon JB, ed. Report of the Rhinosinusitis Task Force Committee Meeting. Otolaryngol Head Neck Surg 1997;117(suppl): S1-S7.

73. Bamberger DM. Antimicrobial treatment of sinusitis. Semin Respir Infect 1991;6:77-84.

74. Dingle JH, Bodger GF, Jordan WS Jr. Illness in the home: a study of 25,000 illnesses in a group of Cleveland families. Cleveland Press: Case Western Reserve University, 1964:347.

75. Williams JW, Simel DL, Roberts L, Samsa GP. Clinical evaluation for sinusitis. Making the diagnosis by history and physical examination. Ann Intern Med 1992;117:705-10.

76. Little DR, Mann BL, Sherk DW. Factors influencing the clinical diagnosis of sinusitis. J Fam Pract 1998;46:147-52.

77. Hueston WJ, Eberlein C, Johnson D, Mainous AG III. Criteria used by clinicians to differentiate sinusitis from viral upper respiratory tract infection. J Fam Pract 1998;46:487-92.

78. Berg O, Carenfelt C, Rystedt G, Änggård A. Occurrence of asymptomatic sinusitis in common cold and other acute ENT infections. Rhinology 1986;24:223-5.

79. Lindbaek M, Hjortdahl P, Johnsen U. Use of symptoms, signs, and blood tests to diagnose acute sinus infections in primary care: comparison with computed tomography. Fam Med 1996;28:183-8.

80. Kankam CG, Sallis R. Acute sinusitis in adults: difficult to diagnose, essential to treat. Postgrad Med 1997;102:253-8.

81. Chow AW, Hall CB, Klein JO, Kammer RB, Meyer RD, Remington JS. General guidelines for the evaluation of new anti-infective drugs for the treatment of respiratory tract infections. Evaluation of new anti-infective drugs for the treatment of respiratory tract infections. Clin Infect Dis 1992;15(suppl 1):S62-S88.

82. Dowell SF, Schwartz B, Phillips WR. Appropriate use of antibiotics for URIs in children. Part I. Otitis media and acute sinusitis. Am Fam Physician 1998;58:1113-8.

83. Stewart MH, Siff JE, Cydulka RK. Evaluation of the patient with sore throat, earache, and sinusitis: an evidence based approach. Emerg Med Clin North Am 1999;17:153-87.

84. Gwaltney JM Jr, Phillis CD, Miller RD, Riker DK. Computed tomographic study of the common cold. N Engl J Med 1994;330:25-30.

85. The Institute for Clinical Systems Integration. Acute sinusitis in adults. Postgrad Med 1998;103:154-6, 159-60, 166-8.

86. Willet LR, Carson JL, Williams JW Jr. Current diagnosis and management of sinusitis. J Gen Intern Med 1994;9:38-45.

87. Williams JW Jr, Simel DL. Does this patient have sinusitis? Diagnosing acute sinusitis by history and physical examination. JAMA 1993;270:1242-6.

88. de Bock GH, Dekker FW, Stolk J, Springer MP, Kievit J, van Houwelingen JC. Antimicrobial treatment in acute maxillary sinusitis: a meta-analysis. J Clin Epidemiol 1997;50:881-90.

89. Gwaltney JM Jr. State-of-the-art: acute community-acquired sinusitis. Clin Infect Dis 1996;23:1209-23.

90. Douville L. Management of acute sinusitis. J Am Acad Nurse Pract 1995;7:407-11.

91. Stafford CT. The clinician's view of sinusitis. Otolaryngol Head Neck Surg 1990;103:870-4.

92. Clayman GL, Adams FL, Paugh DR, Koopmann CF Jr. Intracranial complications of paranasal sinusitis: a combined institutional review. Laryngoscope 1991;101:234-9.

93. Lerner DN, Choi SS, Zalzal GH, Johnson DL. Intracranial complications of sinusitis in childhood. Ann Otol Rhinol Laryngol 1995;104:288-93.

94. Broberg T, Murr A, Fischbein N. Devastating complications of acute pediatric bacterial sinusitis. Otolaryngol Head Neck Surg 1999;120:575-9.

95. Aronovitz GH. Antimicrobial therapy of acute otitis media: review of treatment recommendations. Clin Ther 2000;22: 29-39.

96. Thornsberry C, Ogilvie PT, Holley HP Jr, Sahm DF. Survey of susceptibilities of *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* isolates to 26 antimicrobial agents: a prospective US study. Antimicrob Agents Chemother 1999;43:2612-23.

97. Craig WA. Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men. Clin Infect Dis 1998;26:1-10.

98. Mason EO, Lamberth LB, Kershaw NL, Prosser BLT, Zoe A, Ambrose PG. *Streptococcus pneumoniae* in the United States: in-vitro susceptibility and pharmacodynamic analysis. J Antimicrob Chemother (in press).

99. Marchant CD, Shurin PA, Turcyzk VA, Feinstein JC, Johnson CE, Wasikowski DE, et al. A randomized controlled trial of cefaclor compared with trimethoprim-sulfamethoxazole

for treatment of acute otitis media. Pediatrics 1984;105:633-8.

100. Pichichero ME. Resistant respiratory pathogens and extended-spectrum antibiotics. Am Fam Physician 1995;52:1739-46.

101. Levy DG, Stergachis A, McFarland LV, Van Vorst K, Graham DJ, Johnson ES, et al. Antibiotic and *Clostridium difficile* diarrhea in the ambulatory care setting. Clin Ther 2000;22:91-102.

102. Klein JO. History of macrolide use in pediatrics. Pediatr Infect Dis J 1997;16:427-31.

103. Dagan R, Johnson CE, McLinn S, Abughali N, Feris J, Leibovits E, et al. Bacteriologic and clinical efficacy of amoxicillin/clavulanate vs. azithromycin in acute otitis media. Pediatr Infect Dis J 2000;19:95-104.

104. Pichichero ME. Cefprozil and respiratory tract infections in children. Pediatr Infect Dis J 1998;17:S53-S54.

105. Guay DRP. Formulary management of macrolide antibiotics. Pharmacoeconomics 1995;8:491-512.

106. Lynch JP III, Martinez FJ. Antimicrobial resistance in *Streptococcus pneumoniae*: implications for treatment in the new century. Available at: http://www.medscape.com/Medscape/RespiratoryCare/Treatmentupdate/1999/tu02/public/toc-tu02.html. Accessed February 2, 2000.

107. Doern GV, Pfaller MA, Ervin ME, Brueggemann AB, Jones RN. The prevalence of fluoroquinolone resistance among clinically significant respiratory tract isolates of *Streptococcus pneumoniae* in the United States and Canada — 1997 results from the SENTRY antimicrobial surveillance program. Diagn Microbiol Infect Dis 1998;32:313-6.

108. Jones RN, Biedenbach DJ, Erwin ME, Beach ML, Pfaller MA. Activity of gatifloxacin against *Haemophilus influenzae* and *Moraxella catarrhalis*, including susceptibility test development, E-test comparisons, and quality control guidelines for *H influenzae*. J Clin Microbiol 1999;37:1999-2002.

109. Schmitz FJ, Verhoef J, Fluit AC. Comparative activities of six different fluoroquinolones against 9,682 clinical bacterial isolates from 20 European university hospitals participating in the European SENTRY surveillance programme. The SENTRY participants group. Int J Antimicrob Agents 1999;12:311-7.

110. Balfour JA, Lamb HM. Moxifloxacin: a review of its clinical potential in the management of community-acquired respiratory tract infections. Drugs 2000;59:115-39.

111. Spector SL, Bernstein IL. Parameters for the diagnosis and management of sinusitis. J Allergy Clin Immunol 1998;102 (suppl):S107-S144.

112. Pichichero ME, Cohen R. Shortened course of antibiotic therapy for acute otitis media, sinusitis and tonsillopharyngitis.

Pediatr Infect Dis J 1997;16:680-95.

113. Klapan I, Cŭlig J, Orešković K, Matrapazovski M, Radošević S. Azithromycin versus amoxicillin/clavulanate in the treatment of acute sinusitis. Am J Otolaryngol 1999;20:7-11.

114. Werk LN, Bauchner H. Practical considerations when treating children with antimicrobials in the outpatient setting. Drugs 1998;55:779-90.

115. Polmar SH. The role of the immunologist in sinus disease. J Allergy Clin Immunol 1992;90:511-5.

116. Hardman JC, Limbird LE, Molinoff PB, Ruddon RW, Gilman AG. The pharmacologic basis of therapeutics. 9th ed. New York, NY: McGraw-Hill, 1996.

117. Katcher ML. Cold, cough, and allergy medications: uses and abuses. Pediatr Rev 1996;17:12-7.

118. Zieger RS. Prospects for ancillary treatment of sinusitis in the 1990s. J Allergy Clin Immunol 1992;90:478-95.

119. Ober NS. Respiratory tract infections: consider the total cost of care. Drug Benefit Trends 1998;10:23-9.

120. Thompson D. The costs of antimicrobial treatment failure in acute otitis media. Am J Manag Care 1999;5:S1000-S1003.

121. Hoppe JE. Rational prescribing of antibacterials in ambulatory children. Pharmacoeconomics 1996;10:552-74.

122. Steele RW, Estrada B, Begue RE, Mirza A, Travillion D, Thomas M. A double-blind taste comparison of pediatric antibiotic suspensions. Clin Pediatr 1997(April):193-9.

123. Krouse JH, Krouse HJ. Patient use of traditional and complementary therapies in treating rhinosinusitis before consulting an otolaryngologist. Laryngoscope 1999;109:1223-7.

124. McAlister WH, Lusk R, Muntz HR. Comparison of plain radiographs and coronal CT scans in infants and children with recurrent sinusitis. AJR Am J Roentgenol 1989;153:1259-64.

125. Evans KL. Recognition and management of sinusitis. Drugs 1998;56:59-71.

126. Wald ER, Milmoe GJ, Bowen AD, Ledesma-Medina J, Salamon N, Bluestone CB. Acute maxillary sinusitis in children. N Engl J Med 1981;304:749-54.

127. Evans FO, Sydnor B, Moore WE, Moore GR, Manwaring JL, Brill AH, et al. Sinusitis of the maxillary antrum. N Engl J Med 1975;293:735-9.

128. Lusk RP. Surgical management of chronic sinusitis. In: Lusk RP, ed. Pediatric sinusitis. New York, NY: Raven Press, 1992:77-125.

129. DeBenedictis FM, Bush A. Rhinosinusitis and asthma: epiphenomenon or causal association? Chest 1999;115:550-6.

130. Rachelefsky GS. National guidelines needed to manage rhinitis and prevent complications. Ann Allergy Asthma Immunol 1999;82:296-305.