Chapter 5
Microbiology of Acute, Subacute, and Chronic Rhinosinusitis in Children

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Introduction

An understanding of the microbiology of acute bacterial sinusitis in children is key to making decisions about antimicrobial selection. Most work in this area has focused on acute bacterial sinusitis, with fewer studies addressing subacute and chronic sinusitis in children. Since the routine use of conjugate pneumococcal vaccines in 2000 and the emergence of *Streptococcus pneumoniae* which were highly resistant to penicillin, there has been renewed interest in determining the microbiology and epidemiology of sinusitis. This chapter will focus primarily on the microbiology of acute sinusitis in children. Subacute and chronic sinusitis in children, which have received much less attention in the medical literature, will also be reviewed.

Acute Bacterial Sinusitis

Sinus Aspiration

The challenge in obtaining material for culture is that the sinuses are a closed system accessible only through a mucous membrane that is highly contaminated with respiratory flora. Because of the invasive nature of sinus aspirates, this procedure has not been performed on humans with normal sinuses. The sterility of the sinus cavity has been established in healthy rhesus monkeys that have undergone sinus aspiration [1]. This sterile environment is maintained by the mucociliary apparatus of the sinus and by normal immune function.

Aspiration of the maxillary sinus after sterilization of the mucous membrane of the nasal cavity is the most stringent method for obtaining culture material to avoid contamination. This procedure is performed by anesthetizing and sterilizing the nasal mucosa with a solution of 10 % cocaine (cocaine has antiseptic properties). A culture of the mucosa is performed to test sterility to ensure that effective antisepsis has been achieved. Puncture is performed with a sterile 16-gauge trocar positioned beneath the inferior nasal turbinate; the antral cavity is aspirated. If no material is returned, then the sinus is irrigated with non-bacteriostatic saline which is aspirated and sent for culture. A significant growth of bacteria is considered $\geq 10^4$ colony-forming units per milliliter [2]. Results must be expressed quantitatively to ensure that an organism is present in sufficient number to represent a true pathogen and not a contaminating organism.

The only sinus puncture studies performed in children to establish the microbiology of acute bacterial sinusitis were reported in the 1980s [3, 4] (Table 5.1). Fifty children between the ages of 1 and 16 years who were suspected of having sinusitis were evaluated. Children were entered into the study based on clinical symptoms and abnormal plain radiographs of the maxillary sinuses. Sinus puncture was performed and aspirates were cultured aerobically and anaerobically and a Gram stain prepared. A total of 79 sinus aspirates were performed. At least one sinus had significant growth in 51 of 79

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Table 5.1 Bacteriology of acute sinusitis in 79 sinus aspirates in 50 children with acute sinusitis based on sinus puncture [3, 4]

Organism	Total number of isolates	% of isolates
S. pneumoniae	22	37
H. influenzae[a]	15	25
M. catarrhalis	15	25
Streptococcus species	4	7
Other[b]	3	5
Total	*59*	*100*

[a]All were non-typable

[b]*Eikenella corrodens*, *Peptostreptococcus*, and *Moraxella* sp.

(65 %) aspirates. The predominant organisms isolated from the maxillary sinuses by puncture, in order of frequency, were *Streptococcus pneumoniae*, non-typable *Haemophilus influenzae*, and *Moraxella catarrhalis*. As in studies of otitis media in this era, *S. pneumoniae* was isolated at about 1.5–2 times the rate of isolation of *H. influenzae* and *M. catarrhalis*. It is notable that 13 % of sinus aspirates grew more than one species of bacteria. Six of the 50 subjects had isolates of bacteria that were beta-lactamase producing. This study was also remarkable in that anaerobic bacteria were only present in one aspirate and there were no isolates of *Staphylococcus aureus*.

Endoscopically Obtained Cultures of the Middle Meatus

Because sinus aspiration is not a routine procedure, may be uncomfortable, may rarely be associated with complications, and should only be performed by a pediatric otolaryngologist, there has been a search for a surface culture of the respiratory mucosa, obtained by less invasive methods, which might correlate with the results of the sinus aspirate. The challenge in any less invasive method is that the nasal mucosa is heavily colonized with normal bacterial flora. Cultures of the middle meatus obtained by the use of an endoscope have been used as a surrogate for sinus aspiration. The maxillary, frontal, and anterior air cells of the ethmoid sinuses drain into the middle meatus via the osteomeatal complex. The endoscope is inserted into the nose, and a sample is obtained from material in the middle meatus via a swab or aspiration. The mucosa of the anterior nares must be disinfected, and meticulous care must be taken to be sure the endoscope does not touch the nasal vestibule and become contaminated. Benninger et al. performed a meta-analysis of studies in a mainly adult population comparing endoscopically obtained cultures of the middle meatus to maxillary sinus puncture [5]. When all bacterial isolates are considered, endoscopically obtained cultures show a sensitivity of 80 %, specificity of 70 %, positive predictive value of 78 %, negative predictive value of 75 %, and an overall accuracy of 76 % when compared with maxillary sinus aspiration. If only the sinus pathogens *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* are taken into account, the test performs somewhat better with a sensitivity and specificity of 81 and 83 %, positive and negative predictive value of 91 and 89 %, and overall accuracy of 87 %. Given that the caliber of the nasal passage in children is significantly smaller than adults, one might expect a greater rate of contamination of endoscopically obtained cultures when this procedure is performed in children. Hsin et al. compared endoscopic middle meatal cultures to maxillary sinus puncture in children 2–12 years with subacute and chronic sinusitis [6]. This population of children had failed 30 days or more of antimicrobial therapy. Endoscopic culture performed less well in children than adults with a sensitivity of 75 %, a specificity of 99.9 %, a positive predictive value of 96 %, negative predictive value of 50 %, and an accuracy of 78 %. Overall endoscopic cultures may provide useful information for the treatment of individual adults when interpretation is confined to the three sinus pathogens: *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. However, in epidemiological studies of the etiology of sinusitis, endoscopic cultures are likely to be confounded by normal nasal flora such as alpha-hemolytic streptococci, *Corynebacterium*, and *Staphylococcus* species and, therefore, are of limited usefulness in children.

Surface Cultures

Because of the ease of obtaining a culture of the anterior nose or the nasopharynx, several studies have examined whether the results of these surface cultures corresponded to the results of maxillary sinus aspiration. Axelsson and Brorson studied 472 patients (the age range of the patients was not specified) and found a correlation between the nasal culture and the sinus aspirate only 50 % of the time [7].

In a study done solely in children, nasopharyngeal cultures were taken at the same time as a sinus aspirate was performed [3]. Of 17 subjects who had a predominant organism recovered from the nasopharynx, the same organism was present in the

sinus aspirate in only 4. Thus nasal and nasopharyngeal cultures show a poor correlation with cultures of the sinus performed by aspiration [7]. In contrast, there has been no study to determine if the absence of *S. pneumoniae* on culture of the nasopharynx might have a high negative predictive value regarding the likelihood of *S. pneumoniae* as a cause of sinusitis.

The Role of *Staphylococcus aureus*

In sinus puncture studies, *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* have been identified as the major pathogens associated with acute bacterial sinusitis. Recently, some authors have purported that *S. aureus* should also be considered a major pathogen in acute bacterial sinusitis [5, 8, 9]. If this were the case, it would have important implications for empiric antibiotic selection as current guidelines do not include recommendations for the use of agents that are directed at this pathogen [10, 11]. When examined carefully, however, the role of *S. aureus* as an etiological agent of acute bacterial sinusitis is doubtful [12]. In adults, during a period of 15 years of performing sinus aspirates, *S. aureus* was present in only 7 of 226 (3 %) positive specimens obtained from 339 patients [13]. No isolates of staphylococci were detected in significant quantity in the two studies in which maxillary aspirates were performed in 50 children with acute bacterial sinusitis [3, 4].

The majority of studies arguing that *S. aureus* is a sinus pathogen are based on cultures of the middle meatus. To effectively analyze such studies, it is important to understand the microbiology of the nose and middle meatus in healthy individuals. The nasal vestibule is an area that may be heavily colonized with *S. aureus*. In one study of healthy children in a community setting, over 65 % of children harbored *S. aureus* in the anterior nares [14]. Any study of the microbiology of the middle meatus involves passing an endoscope through this highly colonized region. Thus, even with measures such as antisepsis and the use of a sterile nasal specula, contamination is possible.

The middle meatus itself is also an area densely colonized with bacteria. Gordts et al. performed middle meatal cultures on healthy children who were undergoing surgery for reasons unrelated to the head and neck [15]. In this study, a swab was placed through an ear speculum placed in the disinfected nasal vestibule. Cultures were performed from swabs of the middle meatus and revealed *S. pneumoniae* in 50 %, *H. influenzae* in 40 %, *M. catarrhalis* in 34 %, *S. aureus* in 20 %, and *Corynebacterium* in 52 %. In a study of children with recurrent or chronic sinusitis, *S. aureus* was present in the middle meatus in 32 % of samples [16]. These studies indicate that the middle meatus is heavily colonized with pathogenic and nonpathogenic bacteria in healthy children. Thus, identifying any of these organisms from the middle meatus in children with sinusitis may represent normal colonization and not the etiology of the sinus infection.

Payne et al. performed a meta-analysis on studies of sinus aspirate and middle meatal cultures in adults and concluded that *S. aureus* is prevalent in sinus cultures and should be considered a major pathogen [9]. The authors state that *S. aureus* was found in culture from various sinus and nasal sources 10 % of the time overall. There are significant problems with this analysis, however. First, it is notable that this rate of culture positivity is in the range of results seen in cultures of the middle meatus in healthy adults suggesting that cultures may have been contaminated [17]. Also, in middle meatal cultures, *S. aureus* was isolated at nearly twice the rate as cultures of sinus aspirates (14 % vs 7.8 %). One would expect that these two rates would be similar unless the middle meatal cultures were contaminated with normal flora. In addition, studies included in this meta-analysis had serious methodological problems. For example, in one of the studies with the highest (20 %) rate of isolation of *S. aureus* from sinus aspirates, no methods are given for performing the sinus aspirate [18]. It was not indicated whether the nasal mucosa was disinfected before the procedure. In addition, all patients who had *S. aureus* isolated in this study had anatomic abnormalities of the nasal cavity. This raises serious concerns that the culture results for *S. aureus* may represent contamination from normal nasal flora and thus would skew the results of the meta-analysis.

Overall, caution must be exercised in interpreting these recent studies highlighting the role of *S. aureus* as a major pathogen in acute bacterial sinusitis. Studies in children have mainly relied on middle meatal specimens which do not show good correlation with maxillary sinus aspiration. In the studies in adults, there is serious concern that similar studies have a high rate of contamination with normal nasal flora. It appears unlikely that *S. aureus* is a major pathogen in acute bacterial sinusitis. Accordingly, empiric antibiotic choices need not include coverage for this organism.

The Changing Microbiology of Acute Bacterial Sinusitis

No sinus puncture studies in children with acute bacterial sinusitis have been published since 1984 [4]. Knowledge of changes in the microbiology of acute bacterial sinusitis is important in making decisions about antibiotic selection. In the absence of high-quality data from sinus aspirates, important information may be learned from cultures of middle ear aspirates in children with acute otitis media (AOM). AOM may be used as a surrogate for sinusitis as the middle ear is, in fact, a paranasal sinus [19]. The anatomy and physiology of the middle ear are very similar to that of the sinuses. The middle ear

Table 5.2 Rate of isolation of pathogens from middle ear fluid in children with acute otitis media before and after the introduction of 7-valent pneumococcal conjugate vaccine (PCV-7)

Study	S. pneumoniae		H. influenzae		M. catarrhalis	
	Pre-PCV-7	Post-PCV-7	Pre-PCV-7	Post-PCV-7	Pre-PCV-7	Post-PCV-7
Block, 2004 [20]	48	31	41	56	9	11
Casey, 2004 [21]	48	31	38	57	4	1
Kaur, 2010 [51]	–	25	–	35	–	9

drains via the Eustachian tube into the nasopharynx, analogous to sinus drainage via the osteomeatal complex into the nose. A viral upper respiratory infection is often the predisposing factor for both of these infections causing impairment of drainage with subsequent bacterial growth and inflammation. Like sinusitis, the major pathogens of AOM are *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. Examining the changes of the epidemiology of these pathogens in the context of AOM should reflect similar changes that have occurred in acute bacterial sinusitis.

Since the introduction of the 7-valent pneumococcal conjugate vaccine (PCV-7), there has been a shift in the rate of isolation of *S. pneumoniae* from middle ear fluid in children with AOM (Table 5.2). Two studies have compared the relative rates of isolation of otitis pathogens before and after the introduction of PCV-7 in 2000 for universal immunization in the United States. Block et al. performed tympanocentesis on 381 children aged 7–24 months with otitis media in a practice setting in rural Kentucky [20]. After the introduction of PCV-7, the rate of isolation of *S. pneumoniae* decreased significantly from 48 to 21 % of all isolates. Meanwhile, *H. influenzae* was isolated more frequently during this time period, shifting from 41 to 56 % of isolates. The rate of isolation of *Moraxella* was not changed in this study. In the second study, covering the period from 1995 to 2003, Casey et al. cultured middle ear fluid obtained from children who had failed treatment for AOM or had persistent AOM [21]. During this time period, the rate of isolation of *S. pneumoniae* decreased from 48 to 31 %, *H. influenzae* increased from 38 to 57 %, and *Moraxella* did not change. This same group, however, found a near reversal of this trend between 2007 and 2009 (before the introduction of the 13-valent conjugate pneumococcal vaccine in 2010). During this time frame, *S. pneumoniae* and *H. influenzae* were isolated 44 and 41 % of the time from middle ear fluid [22]. This change was primarily due to the emergence of penicillin-resistant serotype 19 of *S. pneumoniae*. Subsequent data, accumulated by Pichichero et al., suggest that increasing use of PCV-13 has truncated this issue, with a dramatic diminution of cases caused by *S. pneumoniae* [23]. Further assessment of this microbiological shift will be important as the use of PCV-13 becomes more widespread. Overall, we can anticipate that the prevalence *of S. pneumoniae* will continue to decrease and *H. influenzae* increase as the causative organism in children with AOM in the United States. It is likely the same phenomenon is occurring with acute bacterial sinusitis, since the source of the pathogens in both diseases is ultimately the nasopharynx. The proportion of cases of sinusitis caused by *H. influenzae* will drive the selection of an appropriate antibiotic that is beta-lactamase stable.

The prevalence of resistance to the common antimicrobial agents used to treat AOM and acute bacterial sinusitis has varied greatly over the past decade. There has been large geographic variation in penicillin and macrolide resistance rates in *S. pneumoniae* and an increase in ampicillin resistance in *H. influenzae* worldwide mediated by beta-lactamase production. Table 5.3 demonstrates that surveys of respiratory isolates in populations have shown great variation over geographic region and time [20, 22, 24–34]. Historically, the proportion of *H. influenzae* from respiratory sources, including middle ear fluid, that have produced beta-lactamase has been 20–30 %. Recently, nasopharyngeal and middle ear isolates of *H. influenzae* in children from Upstate New York have shown rates as high as 50 % [22], and in Asia rates of 60–65 % have been reported [31]. If these high rates of resistance are widespread, then the effectiveness of amoxicillin as first-line treatment for AOM and acute bacterial sinusitis will be significantly limited.

In the post-PCV-7 era, the rates of isolation of penicillin non-susceptible *S. pneumoniae* (PNSP) have also varied greatly depending on the geographic region and the source of the isolates. The overall trend, however, seems to be either a decrease or no change in the rate of isolation of PNSP since the introduction of PCV-7. Penicillin non-susceptibility rates have ranged from 10 to 61 % [22, 29] (Table 5.3). The Active Bacterial Core surveillance program measured rates of invasive disease caused by PNSP in the United States. Among children under 2 years of age, disease caused by penicillin non-susceptible strains decreased by 81 % from 1999 to 2004, concurrent with the introduction of the pneumococcal conjugate vaccine. During the last two decades, the prevalence of macrolide resistance in *S. pneumoniae* has become widespread, limiting the usefulness of azithromycin and clarithromycin in treating AOM and, by inference, acute bacterial sinusitis. [25] In surveys of surface and middle ear isolates from children, one constant is that *M. catarrhalis* produces beta-lactamase nearly 100 % of the time [22].

Several conclusions may be drawn from these epidemiological studies over the past decade. These data have been derived mainly from middle ear and nasopharyngeal isolates but likely apply to acute bacterial sinusitis. (1) There has been a shift in the proportion of isolation of respiratory pathogens with an increase in the rate of isolation of *H. influenzae* and a decrease

Table 5.3 Rates of antimicrobial resistance (%) in *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*

Study	Population	Source	Region	*S. pneumoniae*	*H. influenzae*		*M. catarrhalis*
				PNSP	Macrolide resistant	Beta-lactamase positive	Beta-lactamase positive
Casey, 2010 [22]	Children	Nasopharynx + middle ear	NY, USA	17–61	–	29–50	100
Harrison, 2009 [29]	Children	Respiratory	USA	10.6	37.3	42	95.2
Gotoh, 2008 [31]	Children	Nasopharyngeal	Vietnam	–	–	59.5	–
Fallon, 2008 [27]	Mainly children	Middle ear fluid	USA	19.4	–	45.5	–
Critchey, 2008 [25]	Children	All – most common serotypes	USA	51	45	–	–
Critchey, 2007 [24]	Adults and children	Respiratory	USA	37.9	34.5	27.4	91.6
Tristam, 2007 [30]	Adults and children	Literature review	Worldwide	–	–	3–65	–
McEllistrem, 2005 [33]	Children	Middle ear fluid	USA	59	–	–	–
Garbutt, 2004 [32]	Children	Nasopharynx	St. Louis, USA	19	63	–	–
Block, 2004 [20]	Children	Middle ear fluid	Rural Kentucky	19		36	100
Gordon, 2003 [28]	Adults and children	Respiratory	USA	35	23	24.5	–
Joloba, 2001 [34]	Children	Middle ear	USA	57	43		
Doern, 1999 [26]	Adults and children	All isolates	USA and Canada	–	–	33.5	99.2

in the isolation of *S. pneumoniae*. (2) The rate of beta-lactamase production by *H. influenzae* has increased. (3) The rate of isolation of penicillin non-susceptible *S. pneumoniae* has either decreased or stayed the same. (4) Macrolide resistance in *S. pneumoniae* is widespread. (5) The rate of isolation of *M. catarrhalis* has remained unchanged and nearly all produce beta-lactamase. These shifts in the microbiology limit the usefulness of amoxicillin for the treatment of acute bacterial sinusitis. Therefore, the addition of clavulanate to amoxicillin provides theoretical advantage in therapy.

Role of Viruses

Although viruses have often been implicated in the pathogenesis of acute bacterial sinusitis, the epidemiology and exact role of viruses have not been well defined. In the original sinus aspiration studies in children in the 1980s, traditional viral cell culture methods were used to identify viruses in sinus samples as well as in throat swabs taken from children with sinusitis [4]. Of 45 children tested, only three had viruses identified on culture. Sinus aspirates grew a parainfluenza virus and an adenovirus, and one throat culture grew a coxsackie B virus. Studies in adults have also isolated rhinovirus in viral culture [13]. No studies of the viruses associated with childhood sinusitis have been reported using molecular techniques nor have any tested for recently recognized respiratory viruses such as human metapneumovirus or bocavirus. It is widely believed that a viral URI is often the prescient event that results in the complication of acute bacterial sinusitis. Thus, an understanding of the viral epidemiology of sinusitis may lead to methods to prevent this infection. Once again using the analogy of AOM is useful in understanding what is occurring during episodes of sinusitis. Studies surveying the viruses associated with AOM using PCR techniques have demonstrated the presence of rhinovirus, respiratory syncytial virus, human metapneumovirus, influenza A and B, parainfluenza virus, adenovirus, human bocavirus, enteroviruses, and coronavirus [35, 36]. It is likely that these same viruses also play a role in the development of acute bacterial sinusitis.

Complications

The rate of complications in children who have sinusitis is relatively low. However, they are associated with serious morbidity and occasional mortality. These complications may be categorized as extracranial, intracranial, and those involving the bone of the sinus wall (osteitis). The extracranial complications include orbital cellulitis and abscess, subperiosteal abscess, optic neuritis, and preseptal inflammatory edema. Epidural and subdural empyema, meningitis, brain abscess, and cavernous sinus thrombosis comprise the intracranial complications of acute bacterial sinusitis. Pott's puffy tumor is an osteitis of the wall of the frontal sinus that presents with forehead swelling and tenderness. Since many of these complications of sinusitis

Table 5.4 Microbiology of the orbital and intracranial complications of sinusitis

	Orbital (125 isolates)	Intracranial (142 isolates)
Gram positive		
S. aureus	58	6
S. pneumoniae	2	4
S. anginosus	4	49
S. pyogenes	9	9
Other β-hemolytic streptococci	1	4
Other α-hemolytic streptococci	14	20
Coagulase-negative staphylococci	4	12
Other gram positive		1
Gram negative		
Enteric gram-negative rods	9	5
NTHi	6	2
Other *Haemophilus* spp.	2	1
M. catarrhalis		1
Neisseria spp.	2	
Anaerobes		
Bacteroides spp.	1	6
Eikenella spp.	3	2
Fusobacterium spp.	3	3
Peptostreptococcus	3	6
Prevotella	1	2
Other	3	9

From Refs. [37–45]

are local fluid collections, surgical drainage is necessary. Specimens sent for culture from these sources are likely to represent the actual etiology of the infection.

A summary of the studies that have surveyed the microbiology of the orbital and intracranial complications of sinusitis is shown in Table 5.4 [37–45]. In orbital infections, *Staphylococcus aureus* is the predominant pathogen followed by *Streptococcus pyogenes*, *S. pneumoniae*, other gram positives, *H. influenzae*, enteric gram-negative bacilli, and anaerobes. The importance of methicillin-resistant *S. aureus* in orbital disease has been increasingly recognized [45]. In intracranial complications, the microbiology is similar, though *S. aureus* is isolated less frequently than in orbital infections. Over the past decade, *Streptococcus anginosus* (formerly *S. milleri*) has become the predominant pathogen isolated in many studies.

Subacute and Chronic Sinusitis

Much less attention has been given to the microbiology of subacute and chronic sinusitis in children. This is complicated, in part, by a lack of standard definitions for these conditions. Acute sinusitis has been defined as an infection with a duration of less than 4 weeks. Subacute sinusitis is infection from 4 weeks to 2–3 months. Chronic sinusitis is commonly defined as infection for more than 2–3 months and often years [46]. These definitions, however, are somewhat arbitrary.

Wald studied the microbiology of children with subacute sinusitis. Children aged 2–16 had sinus symptoms for more than 30 but less than 120 days. Maxillary sinus aspirations were performed on 52 sinuses in 40 children with significant bacterial growth found in 58 % of these aspirates. The organisms isolated included *S. pneumoniae* (34 %), *H. influenzae* (31 %), and *M. catarrhalis* (23 %) with the remainder comprised of Group A beta-hemolytic streptococci, viridans streptococci, and a *Moraxella* species. Of the *H. influenzae* isolated, 27 % were beta-lactamase producing and many of the children in the study had recently received antibiotics. Overall, the microbiology of these children with subacute sinusitis was nearly identical to those with acute bacterial sinusitis.

Available microbiologic data from children with chronic sinusitis are limited and confusing because of variable definitions of chronic sinusitis, frequent failure to obtain specimens aseptically, lack of quantitation of results, and concurrent use of antibiotics. In children with chronic sinusitis, multiple species of bacteria have been isolated from sinus aspirates. Brook found anaerobic bacteria such as *Bacteroides*, anaerobic gram-positive cocci, and *Fusobacterium* species predominated among these isolates [47]. Aerobic bacteria were isolated less frequently and included alpha-hemolytic streptococci, *S. aureus*, and *Haemophilus* species. In a separate study of acute exacerbations of chronic sinusitis, multiple species of anaerobes, *H. influenzae*, *S. pneumoniae*, *M. catarrhalis*, and *S. aureus* were present [48]. Hsin performed maxillary sinus

puncture in 21 children who had four or more weeks of sinus symptoms despite antimicrobial therapy [6]. This study was somewhat limited in that there was no quantitation of bacterial growth and no sterility testing of the puncture site. However, 28 sinus aspirate cultures demonstrated *S. pneumoniae* (12 aspirates), *H. influenzae* (7 aspirates), *M. catarrhalis* (1 aspirate), and no growth in 5 aspirates.

In patients with chronic persistent sinusitis (nasal congestion and/or rhinorrhea and/or cough), the role of bacteria is less clear. The persistence of symptoms despite multiple courses of appropriate antimicrobial agents is counter to the notion that bacterial infection is a significant component of chronic sinusitis. All these observations support the hypothesis that bacterial infection has a minor role, if any, in a substantial number of patients with chronic sinusitis.

This disease is now thought to be an inflammatory disorder rather than a primary infectious disease [49]. An alternative hypothesis regarding the importance of bacterial infection in patients with chronic sinusitis relates to the potential role of biofilms (discussed in the Chap. 7). Biofilms are complex colonies of bacterial cells that live within a glycocalyx matrix attached to a moist surface. Biofilms offer important survival advantages to bacteria. They are more resistant to the effects of antibiotics than free-floating planktonic bacteria. This is accomplished by several mechanisms: (1) greater cell-cell contact to facilitate plasmid exchange for the evolution of resistance, (2) production of beta-lactamases, (3) slow bacterial growth resulting in decreased effect of antibiotics that rely on cell growth and turnover for killing effect, and (4) the presence of "persister" cells that reform the biofilm when the antibiotic is discontinued [50]. The appeal of the concept of biofilms is that it might explain the chronic nature of the infection, frequent failure to respond to antibiotics, and acute exacerbations when antibiotics are discontinued in patients who had previously responded. Although biofilms have been demonstrated on the mucosa of patients with chronic sinusitis, their precise role remains to be determined as they are not present in all cases of CRS and limited biofilms are present in some healthy controls.

Conclusion

The microbiology of sinusitis in children is dynamic, having undergone significant changes in the past decade. Although there have been no puncture studies done in children since the 1980s, there is evidence that the prevalence of *H. influenzae* relative to *S. pneumoniae* has been increasing since the introduction of the pneumococcal conjugate vaccine in the United States. In addition, the rate of beta-lactamase production by *H. influenzae* is increasing in many areas. Thus, selecting an antimicrobial that is beta-lactamase stable or has a beta-lactamase inhibitor is important in treating children with sinusitis. Future studies that address methods of noninvasively detecting bacteria in the sinus would be helpful so that changes in the microbiology may be more readily monitored. Furthermore, additional research is needed to explore the role of viruses in the pathogenesis of AOM in children.

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