VIEWPOINTS

Staphylococcus aureus: Is It a Pathogen of Acute Bacterial Sinusitis in Children and Adults?

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***Streptococcus pneumoniae, Haemophilus influenzae*, and *Moraxella catarrhalis* are the etiologic agents of acute bacterial sinusitis (ABS). *Staphylococcus aureus* has been an uncommon cause of ABS despite its frequent occupancy within the anterior nares. A quantitative culture of a maxillary sinus aspirate is the gold standard for determining etiology of ABS. Cultures of the middle meatus cannot be used as a surrogate for a maxillary sinus aspirate in children with ABS, although they may be used in adults if interpretation is confined to usual sinus pathogens. Recent studies highlighting *S. aureus* as a major pathogen in ABS should be interpreted cautiously. Most isolates in recent pediatric studies were derived from cultures of the middle meatus. The range of reported results for the incidence of *S. aureus* as a cause of ABS in adults is similar to the results reported for staphylococcal colonization of the middle meatus in healthy adults.**

Acute bacterial sinusitis is a common and costly clinical problem in both children and adults. Sinusitis affects >15% of the US population annually and results in >$5.8 billion in direct healthcare expenditures, of which $1.8 billion is spent on children ≤12 years of age [1]. The microbiology of acute bacterial sinusitis has been thoroughly studied in adult patients; however, in children, there has not been a study of the microbiology of acute sinusitis since 1984 [2]. The traditional and well-established pathogens of acute sinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* [2, 3]. The role of *Staphylococcus aureus* as a pathogen in acute bacterial sinusitis in children and adults has been minimal despite the fact that it is a ubiquitous microorganism, occupying the anterior nares of nearly one-third of the human population at any given time [4]. It is precisely this position in the anterior nares that has made interpretation of the recovery of *S. aureus* from patients with uncomplicated sinus disease so difficult. In contrast, there is an established role for *S. aureus* as a pathogen in patients (both children and adults) with chronic sinusitis and those with suppurative intracranial or intraorbital complications of sinusitis [5–7]. The implications of considering *S. aureus* as a likely cause of acute bacterial sinusitis in a child or adult bear directly on selection of empiric antimicrobials for treatment.

MAXILLARY SINUS ASPIRATION

The best measure or gold standard for describing the microbiology of acute bacterial sinusitis is performance of a maxillary sinus aspirate [3, 8, 9]. To obtain clinically interpretable results, these samples must be retrieved without contamination from the heavily colonized nasal cavity. Accordingly, the area in the nose beneath the middle turbinate, through which the trocar is passed, must be sterilized topically. A test-of-sterility culture should be performed to certify that effective antisepsis has occurred. To further assure that bacteria recovered from sinus aspirates represent in situ infection rather than contamination arising from the nose, the bacteria should be present in high density, that is, a density of 10^4 colony-forming units (CFU) per milliliter [10]. This requires that quantitative bacteriology be performed.

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If cultures are not obtained aseptically and expressed quantitatively, the results may not reliably predict either that infection is truly present or the correct identification of the infecting bacterial species.

Unfortunately, maxillary sinus aspiration in children is a time-consuming procedure that may cause some discomfort, is associated with rare but serious complications, and should be performed only by a pediatric otolaryngologist [11]. In young children, sedation will almost always be required for the safe performance of the procedure. For all of these reasons, there has been substantial interest in identifying a superficial culture of the upper respiratory tract, the results of which would correlate closely with those of a maxillary sinus aspirate.

SURFACE CULTURES AS A SURROGATE FOR MAXILLARY SINUS ASPIRATION

Numerous studies have evaluated the correlation of nasal, nasopharyngeal, and pharyngeal cultures for their ability to predict the results of cultures of the maxillary sinus aspirate. Results have shown uniformly that surface cultures and culture of the maxillary sinus aspirate are not highly correlated [12, 13]. There has been no evaluation of whether nasopharyngeal cultures might have a high negative predictive value for *S. pneumoniae* as they do in cases of acute otitis media [14, 15].

CULTURES OF THE MIDDLE MEATUS AS A SURROGATE FOR MAXILLARY SINUS ASPIRATION

Because of the poor correlation of these surface cultures with those of the maxillary sinus aspirate, there has been particular interest in assessing cultures obtained from the middle meatus. Although this area is not accessible to the primary care practitioner (and therefore use of this site for culturing is not helpful in the primary care setting), it is attractive because it represents the confluence of the maxillary, anterior ethmoid, and frontal sinus outflow tracts; obtaining a culture of the middle meatus is less invasive than maxillary sinus aspiration. However, when cultures are obtained from the middle meatus as a surrogate for cultures of the maxillary sinus aspirate, care should be taken to avoid contamination from the nasal vestibule. This can be accomplished by disinfection of the nasal vestibule with an antiseptic solution such as 4% cocaine or betadine (with proof of decontamination) and use of a sterile nasal speculum, if possible, to further avoid contamination from the anterior nares.

In the study of cultures obtained from the middle meatus, there are 2 questions of importance. First, what is the bacteriology of the middle meatus in subjects who are healthy? Second, what is the correlation of cultures obtained from the meatus compared with the maxillary sinus aspirate? Again, in assessing this comparison, we must be cognizant of the rigor necessary to obtain these cultures with minimal to no contamination from the nasal cavity.

Cultures of Middle Meatus in Healthy Children

There is only a single study in which cultures of the middle meatus have been performed in children [16]. Fifty children undergoing minor surgical procedures unrelated to the respiratory tract were evaluated while under general anesthesia. The nasal mucosa was prepared with oxymetazoline to achieve decongestion. The skin of the nasal vestibule was disinfected with chlorhexidine. Additional contamination was avoided by using a sterile ear speculum to bypass the nasal vestibulum when the specimen was obtained. Bacteria were cultured from the middle meatus of all children (Table 1). The 3 traditional sinus pathogens *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* were very commonly found. In addition, *S. aureus*, viridans streptococci, coagulase-negative staphylococcus, and *Corynebacterium* species were also recovered very often. Given the high prevalence of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* in this population of normal children, the performance of cultures of the middle meatus to predict the cause of acute sinusitis in acutely infected children cannot be recommended.

There have been no studies attempting to correlate cultures of the middle meatus and maxillary sinus aspirates in children with acute bacterial sinusitis.

Cultures of Middle Meatus in Healthy Adults

Summarized in Table 2 are 5 studies that have evaluated cultures of the middle meatus in healthy adults [17–21]. The recovery of bacteria was very common in each of the investigations, ranging from 68% to 94% of patients. The most common bacterial species recovered in each study was coagulase-negative staphylococci followed by *S. aureus* and *Corynebacterium* species. In studies in

Table 1. Bacteria Cultured From the Middle Meatus of 50 Healthy Children

Bacterial Species	Percentage
Haemophilus influenzae	40
Moraxella catarrhalis	34
Streptococcus pneumoniae	50
Streptococcus pyogenes	8
Staphylococcus aureus	20
Streptococcus viridans	30
Neisseria species	14
Coagulase-negative staphylococcus	30
Corynebacterium species	52
Bacillus species	16
Peptostreptococcus species	10
Fusobacterium nucleatum	2

Adapted with permission from Gordts et al [16].

Table 2. Cultures of the Middle Meatus in Healthy Adults

Reference	Patients, No.	Female, %	Mean Age, years	Disinfection Technique	Positive Culture, %	Coagulase-Negative Staphylococcus, %	*Staphylococcus aureus*, %	*Corynebacterium* Species, %	*Proprionobacterium* Acnes, %	Other, %
17	139	47	42	No disinfection; focused sampling	81	53	14	24	13	3
18	25	48	29	No disinfection; focused sampling	68	32	24	20	12	0
19	52	62	24	Skin disinfected with chlorhexidine; sterile speculum	75	35	8	23	7	0
20	18	39	37	Sterile speculum	100	72	22	0	0	18
21	70	57	29	Povidone/iodine ×10 minutes	94	61	12	9	0	3

which careful anaerobic cultures were performed, *Propionobacterium acnes* was recovered in 12%–27% of adults. The striking finding in this series is the recovery of *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis* from only a minority of patients in 1 of the 5 studies [20].

Correlation of Cultures of the Middle Meatus and Maxillary Sinus Aspirate in Adults With Acute Bacterial Sinusitis

Benninger et al [22] reported on the correlation of endoscopically directed cultures of the middle meatus and maxillary sinus aspirates in adults with acute bacterial sinusitis in 3 published studies, 1 abstract, and 2 additional sources of unpublished data [22–25]. Although the authors conclude that endoscopically directed cultures of the middle meatus are highly sensitive and accurate as surrogate cultures of the maxillary sinus aspirate, this enthusiasm must be qualified.

In 1 of the studies included in the meta-analysis, there were no inclusion criteria enumerated and there was no attempt to reduce the likelihood of contamination of the cultures obtained from the middle meatus or the aspirates obtained by the sublabial route [24]. Thirteen of 16 patients were on antibiotics at the time cultures were obtained. The authors did not define what might have been considered a true pathogen or a contaminant. Although *S. aureus* was recovered from 4 cultures of the maxillary antrum, it was present in a significant density in only 1 patient. Typical sinus pathogens were recovered from the antral cultures of 9 of 16 patients. In each of these patients, the same bacterial species appeared in the endoscopic culture.

In the study by Talbot et al [25], 46 patients were evaluated by both nasal endoscopy and sinus puncture. Only 50% of maxillary sinus aspirates were positive, reflecting, at least in part, the relatively nonspecific criteria used to admit patients to the study (without any requirement for a specific duration of respiratory symptoms). In their first analysis, which included all assessable patients and all bacterial species (with the exception of coagulase-negative staphylococci) with a colony count of $>10^3$ CFU/mL in the maxillary sinus aspirate as pathogenic, endoscopy provided a sensitivity of 71.4% (95% confidence interval [CI], 42.0–90.4), specificity of 53.1% (95% CI, 35.0–70.5), positive predictive value of 40.0% (95% CI, 21.8–61.1), negative predictive value of 81.0% (95% CI, 57.4–93.7), and accuracy of 58.7% (95% CI, 43.3–72.7) compared with the gold standard of sinus puncture. When considering only *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae* as pathogens, regardless of colony count, the respective percentages improved substantially to 85.7%, 90.6%, 80%, 93.5%, and 89.1%.

The study by Joniau et al [23] evaluated 24 patients. The maxillary sinus aspirate was performed after decongestion and careful sterilization of the nasal vestibule and the area beneath the inferior turbinate. The maxillary sinus aspirate was obtained using meticulous technique to avoid nasal contamination. The correlation of isolates showed a sensitivity of 80%, specificity of

100%, positive predictive value of 100%, a negative predictive value of 78.6%, and a correlation of 88.5%, compared with the maxillary sinus aspirate. No staphylococcal species were recovered from any specimen.

Benninger et al abstracted data on 10 patients from an unpublished report by Ferguson and Straka [22]. Preparation of the nose was not described for the maxillary sinus aspirates, although the cultures obtained endoscopically were retrieved with use of a secretion collector with a withdrawable sleeve, intended to reduce contamination. No quantitation was performed. Results were discrepant in 2 of 8 pairs of cultures not including the recovery of *S. aureus* and in 2 of 10 pairs when *S. aureus* was included.

Finally, from an additional unpublished data set (26 pairs of cultures evaluated in the context of an industry-sponsored trial), Benninger et al reported a sensitivity of 62.5% (95% CI, 29%–96%) [22]. Eighteen of the 26 cultures showed no growth, raising concerns regarding the quality of entry criteria.

In conclusion, the cumulative results of this study suggest that cultures of the middle meatus in adult patients may be used as a reasonable surrogate for cultures of the maxillary sinus aspirate in adult patients with acute bacterial sinusitis as long as the interpretation of results are confined to the usual sinus pathogens. These results cannot be translated to interpretation of cultures for *S. aureus* or coagulase-negative staphylococci, which most would consider to be nasal contaminants. Furthermore, in children, cultures of the middle meatus have not been shown to be of any value in the evaluation of children with acute bacterial sinusitis.

REINTERPRETATION OF RECENT STUDIES CLAIMING THAT *S. AUREUS* IS A MAJOR PATHOGEN IN ACUTE BACTERIAL RHINOSINUSITIS

Three recently published studies have heightened awareness of the potential role of *S. aureus*, in particular methicillin-resistant *S. aureus* (MRSA), as a pathogen in acute bacterial sinusitis [26–28]. However, these results must be interpreted cautiously.

One study of MRSA in acute rhinosinusitisevaluated 600 outpatients, including 309 children [26]. Cultures were obtained from the middle meatus. The nasal cavity was disinfected with aqueous hibitane and the specimen was obtained through a sterile speculum. Twenty-three isolates (7%) of *S. aureus* and 9 of MRSA were found. Multiple pathogens (the usual sinus isolates) were recovered from 6 of the 9 children with MRSA. Three of the infections were not treated with agents that would be expected to cover MRSA; 2 of the children recovered uneventfully, whereas the third was lost to follow-up. In the absence of any data to suggest that cultures of the middle meatus are valuable in predicting the cause of acute sinus disease in children, these results, which are modest to begin with, should be viewed with skepticism.

Whitby et al performed a retrospective study reporting on isolates of *S. aureus* that were identified in children during an ongoing surveillance study [27]. Fifty-nine isolates of *S. aureus* were identified from 56 patients over a 4-year period. Criterion for inclusion was the isolation of *S. aureus* from a sinus culture. Isolates from 52 of the 56 children were obtained endoscopically. The remaining 4 were from children with complicated sinus infections. In the majority of cases (77%), *S. aureus* was accompanied by a usual sinus pathogen (*H. influenzae* or *S. pneumoniae*). The indication for obtaining cultures was unknown (specifically, it was not indicated whether the children had acute or chronic infections or what the criteria might have been for those diagnoses), and the preparation of the nose before sampling (to eliminate nasal colonization with *S. aureus*) is also undocumented. The likelihood that many of these isolates represent nasal contamination rather than actual infection is substantial. Accordingly, this publication should not be viewed as supporting the conclusion that *S. aureus* is a common or important cause of uncomplicated acute sinus infections in children.

Finally, Payne and Benninger [28] recently published a meta-analysis purported to demonstrate that *S. aureus*, historically an infrequent cause of acute bacterial sinusitis in adults [3], is now a major pathogen in acute bacterial rhinosinusitis. Twenty-six studies performed between 1990 and 2006 were included and showed a wide range for the retrieval of *S. aureus* from adult patients with acute sinusitis over the last 2 decades. Of note, the range of results is similar to those obtained when the middle meatus is cultured in healthy adults (Table 2). Accordingly, interpretation is difficult. As an example, we can review 2 studies included in the meta-analysis that reported the highest incidence of *S. aureus* as an infecting pathogen, 20.5% and 30.8%, respectively [29, 30]. One hundred patients were enrolled in the study reporting 30.8% recovery of *S. aureus*; bacteriologic assessments were performed in only 70 (no explanation provided), approximately one-third of which were negative [29]. Most data were derived from the performance of maxillary sinus aspirates. The technique used for performance of the maxillary sinus aspirate and any preparation of the nose was omitted from the description of methods. When commenting upon the high incidence of recovery of *S. aureus* in the discussion, the authors note that all patients with *S. aureus* as a single pathogen had anatomic abnormalities of the nasal cavity, suggesting the presence of a subacute or chronic form of illness. Furthermore, they comment, ''although all precautions were taken to avoid the contamination of specimens with nasal flora, this possibility could not completely be ruled out'' [29].

The study by Sydnor et al [30], reporting the 20% incidence of recovery of *S. aureus*, was a multicenter investigation involving 329 patients conducted in 24 different centers. Three hundred patients were clinically evaluable and only 138 (42%) were microbiologically evaluable (no explanation was provided).

In 115 patients, cultures were obtained by sinus aspiration and in 23 patients cultures were obtained endoscopically. *S. aureus* was recovered from 16% of the sinus aspirates and 44% of the cultures obtained endoscopically. Preparation of the nose for either sinus aspiration or endoscopy was not reported; quantitation of results was not performed. The authors note only that the prevalence of *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis* is in accordance with previously published microbiologic findings concerning sinusitis. Again, the likelihood of nasal contamination of the sinus aspirates and endoscopically obtained cultures is high.

CONCLUSIONS

The best measure for describing the microbiology of acute bacterial sinusitis is a quantitative culture of a maxillary sinus aspirate that has been performed with great care to avoid nasal contamination. Cultures of the nose, throat, or nasopharynx cannot be used as surrogates for a maxillary sinus aspirate. Cultures of the middle meatus cannot be used as a surrogate for maxillary sinus aspiration in children with acute bacterial sinusitis. Cultures of the middle meatus may be used as a reasonable surrogate for a maxillary sinus aspirate in adults with acute bacterial sinusitis if interpretation is confined to the recovery of the usual sinus pathogens: *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. Recent studies highlighting the importance of *S. aureus* as a major pathogen in children and adults with acute bacterial rhinosinusitis should be interpreted cautiously. The majority of isolates in the studies of children were derived from cultures of the middle meatus that have not been established as a reliable surrogate for maxillary sinus aspirates in children. The range of reported results for the incidence of *S. aureus* as a cause of acute bacterial sinusitis is similar to the range of results reported for staphylococcal colonization of the middle meatus in healthy adults. Accordingly, empiric therapy for patients with acute uncomplicated bacterial sinusitis does not need to include coverage for *S. aureus*.

Note

Potential conflicts of interest. Author certifies no potential conflicts of interest.

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