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Pathogen Yield and Antimicrobial Resistance Patterns of Chronic Rhinosinusitis Patients Presenting to a Tertiary Rhinology Centre

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ABSTRACT

Objectives: **To examine the yield and resistance profile of pathogens in chronic rhinosinusitis (CRS) patients receiving culture-directed management and to pay particular attention to the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) in this population.**

Study Design: **Retrospective review of a CRS microbiology database.**

Participants: **Consecutive CRS patients seen at the St. Paul's Sinus Centre between June 2007 and August 2008.**

Setting: **Canadian tertiary sinus centre.**

Main Outcome Measure: **To determine the pathogens isolated, the frequency of these pathogens, and their resistance profiles.**

Results: **The most common bacterial pathogens isolated were *Staphylococcus aureus*, accounting for 39% of cultured samples, followed by *Haemophilus influenzae* (29%), *Pseudomonas aeruginosa* (15%), *Streptococcus pneumoniae* (12%), and *Moraxella catarrhalis* (11%). Only three cases of MRSA were found, one in a patient with cystic fibrosis.**

Conclusion: **MRSA does not appear to pose a significant risk of morbidity in our patient population. However, ongoing concern regarding the increasing prevalence of *S. aureus* and antimicrobial resistance in chronic sinonasal disease highlights the importance of using culture-directed antimicrobial therapy with the goal of minimizing future resistance patterns.**

SOMMAIRE

Objectifs: **L'étude avait pour objectifs d'examiner la prolifération de micro-organismes pathogènes et leur forme de résistance chez des patients souffrant d'une rhinosinusite chronique (RC) et traités en fonction des résultats des cultures bactériennes, et de porter une attention particulière à la prévalence de *Staphylococcus aureus* résistant à la méthicilline (SARM) dans ce groupe particulier de malades.**

Type d'étude: **Il s'agit d'un examen rétrospectif d'une base de données en microbiologie, sur la RC.**

Participants: **Les participants étaient des patients atteints d'une RC et traités au St. Paul's Sinus Centre, entre juin 2007 et août 2008.**

Lieu: **L'étude a été menée dans un centre canadien de soins tertiaires des maladies des sinus.**

Principaux critères d'évaluation: **Les principaux critères étaient l'identification des micro-organismes pathogènes isolés, leur fréquence ainsi que leur profil de résistance.**

Résultats: **Les micro-organismes pathogènes isolés le plus souvent étaient *Staphylococcus aureus*, qui représentait 39% des échantillons cultivés, suivi d'*Haemophilus influenzae* (29%), de *Pseudomonas aeruginosa* (15%), de *Streptococcus pneumoniae* (12%) et de *Moraxella catarrhalis* (11%). Seuls trois cas de SARM ont été observés, dont l'un chez un patient atteint de fibrose kystique.**

Conclusion: **La bactérie SARM ne semble pas présenter un risque important de morbidité dans la population à l'étude. Cependant, l'augmentation de la prévalence de *S. aureus* et de la résistance aux antimicrobiens dans la maladie nasosinusale**

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Presented at the 2009 Rhinology World Conference, Philadelphia, PA, April 17, 2009.

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DOI 10.2310/7070.2011.100199

chronique se fait préoccupante et met en relief l'importance du traitement antimicrobien fondé sur les cultures bactériennes, et ce, afin de diminuer le plus possible l'apparition de nouvelles formes de résistance.

Key words: *antimicrobial resistance, chronic rhinosinusitis, methicillin-resistant* Staphylococcus aureus

The presence of bacterial infection in the nose and sinuses is thought to be a major contributor to the pathogenesis of both acute and chronic rhinosinusitis (CRS).[1,2] As the growing body of literature suggests, the pathogenesis of bacteria in sinonasal disease may be more complicated than currently understood. Several new theories, particularly those of biofilms covering the sinus mucosa and offering bacteria protection under a complex cellular polymeric substance, have highlighted the complexity of antimicrobial resistance in sinonasal disease.[2] They have also highlighted the need for topical and pressurized therapy to break down the polymeric matrix while eradicating the bacteria in a more direct, nonsystematic manner.

Staphylococcus aureus, a gram-positive bacterium, is among the most common isolates in nasal sinus swabs.[3] This pathogen has been reported to give rise to infections at multiple sites throughout the body, with the nose serving as the primary site in many situations.[4,5] In addition to being involved in several pathogenic processes, studies have isolated *S. aureus* in noninfected sinuses, making its role as a true pathogen debatable in certain clinical contexts.[6] Although previously sensitive to penicillin, many strains of *S. aureus* have developed the ability to produce β-lactamase, an enzyme capable of breaking down penicillin.[4] The ability of *S. aureus* to develop resistance has become increasingly alarming, with some resistant strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA),[4,7] capable of evading almost all antimicrobials available. In many surgical settings, the presence of antimicrobial infections has been linked to poor postoperative outcomes.[5] These increasing concerns, particularly with MRSA, have resulted in a growing need to determine antimicrobial resistance in sinonasal infection.

Traditionally, the mainstay of treatment in chronic rhinosinusitis has been the use of broad-spectrum antibiotics for 4 to 6 weeks.[8–10] Recently, this practice has been suggested to result in increased resistance patterns.[10] The use of culture-directed therapy is being encouraged as the "gold standard" for the management of sinonasal disease.[1] Culture-directed therapy is used in an effort to prevent the further development of resistant strains and provide effective antimicrobial therapy.[9] This practice involves obtaining microbial cultures prior to the onset of therapy and choosing effective antibiotics in accordance with antimicrobial sensitivity profiles.

The primary aim of this study was to examine the yield of pathogens and determine the effectiveness of culture-directed management in patients with CRS presenting to a tertiary sinus centre.

Materials and Methods

Sampling Techniques

A retrospective chart review of CRS patients seen at a tertiary rhinology centre was carried out for the 13-month period between June 2007 and August 2008. All CRS patients who had purulent discharge seen on endoscopic examination had samples taken using one of three methods: a sterile calcium alginate tipped swab, a Lukens trap (Busse Hospital Disposables, Hauppauge, NY), or a sinus secretion collector (Medtronic Xomed Surgical Products, Jacksonville, FL). In most patients, nasal decongestant or analgesic spray was not used. When a swab was used, it was carefully placed in contact with the purulence for at least 10 seconds until moist and then carefully removed without contamination from the nasal wall. If suction traps were used, the tip was placed within the purulence or inside the sinus cavity in which pus was collecting. The samples were then sent to the hospital microbiology laboratory within 30 minutes of capture for culture, Gram stain, and mycology.

Culturing Techniques

All samples were cultured and analyzed according to our hospital laboratory's standard of care technique.[11] Antimicrobial sensitivity was determined in accordance with the National Committee for Clinical Laboratory Standards (NCCLS).[12,13] Bacteria growth was recorded semiquantitatively using the following scale: 1+, few; 2+, moderate; 3+, heavy growth. All cultures were read at 24 and 48 hours and, if negative, were read again on days 3, 4, and 5.

Ethical Considerations

This study was a retrospective chart review of the St. Paul's Hospital Microbiology Log. All patients received treatment

according to our hospital's standard of care. No experimental procedures were performed in this study.

Results

One hundred sixty-eight samples were collected from 132 patients over the 13-month enrolment period (June 2007–August 2008). Seven patients were diagnosed with comorbid cystic fibrosis and four patients with Wegener granulomatosis. The mean age was 51 years (range 22–88 years). There were 65 males and 67 females. Patients were cultured on average 1.27 ± 0.81 times (range 1–7 times) during the enrolment period. When looking at all isolates, the maxillary sinus was the most common site of purulence. The site of culture was not recorded for 47 samples. Bilateral sinuses were cultured in 123 samples. Multiple organisms were cultured in 33 samples. The most common bacterial species identified included *S. aureus* (39%), *Haemophilus influenzae* (16%), *Pseudomonas aeruginosa* (9%), *Streptococcus pneumoniae* (7%), and *Moraxella catarrhalis* (7%) (Figure 1). Quantitative bacterial yield (Table 1) revealed that 75% of the *S. aureus* samples had moderate to heavy growth.

Three samples cultured MRSA, one from a patient with cystic fibrosis. The incidence of MRSA in the entire cohort was 2%. Sensitivity profiles for *S. aureus*, *P. aeruginosa*, *S. pneumoniae*, and *M. catarrhalis* can be found in Figure 2. Eighty-seven percent of *S. aureus*–positive samples were resistant to penicillin G, followed by 14% to erythromycin and 12% to clindamycin (Figure 3). Ten percent of *H. influenzae*–positive samples tested were resistant to ampicillin. *P. aeruginosa*–positive samples showed variable resistance to ceftazidime, tobramycin, ciprofloxacin, piperacillin-tazobactam, meropenem, and trimethoprim-sulfamethoxazole (TMP-SMX). All *M. catarrhalis*–positive samples tested showed resistance to ampicillin. Fifty percent of *S. pneumoniae*–positive samples showed resistance to either erythromycin or penicillin G.

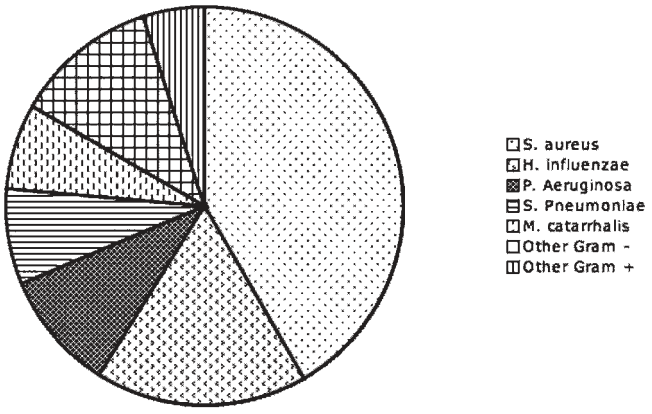

Figure 1. Bacterial pathogens isolated.

Table 1. Quantitative Yield of Bacterial Purulence Captured from Nasal Sinuses

Pathogen	*Heavy Growth*	*Moderate Growth*	*Light Growth*
Staphylococcus aureus	37*	12*	16
Streptococcus pneumoniae	8	3	1
Coagulase-negative *Staphylococcus*	0	3	2
Haemophilus influenzae	12	7	8
Moraxella catarrhalis	5	2	4
Other gram negative	7	7	4
Other gram positive	3	2	3

*Methicillin-resistant *S. aureus* was isolated from two samples (one as heavy growth, the other as moderate growth).

Twenty-one patients were cultured on multiple occasions. Of these patients, 12 (57%) cultured different organisms on repeat culture and 9 (43%) cultured the same organism. The recurrent organisms in these 9 patients included *S. aureus* (70%), *P. aeruginosa* (10%), *S. pneumoniae* (10%), and *H. influenzae* (10%) (Figure 4).

Discussion

The growing concern of antimicrobial resistance, in particularly that of MRSA, has led many investigators to question its importance in sinonasal disease. Several authors have documented increasing rates of antibacterial resistance, most notably the emergence of MRSA in both the hospital and community settings.[4,10,14,15] In this study, antimicrobial-resistant strains were seen in *S. aureus*, *H. influenzae*, *P. aeruginosa*, *S. pneumoniae*, and *M. catarrhalis*.

The role of *S. aureus* and its increasing prevalence in sinonasal disease have been heavily debated in the literature.[3] Several studies have reported *S. aureus* to be among the most common bacteria isolated in chronic sinonasal disease.[1,6,16–20] In keeping with the literature, our study noted that *S. aureus* was the most frequent pathogen isolated and accounted for 39% of culture-positive samples.

Controversy remains as to whether *S. aureus* represents a true pathogen in sinonasal disease or simply a potential commensal of the sinus cavities. Nadel and colleagues suggested that the pathogenicity of *S. aureus* can be linked to the quantity of isolate captured.[6] In their study, they felt

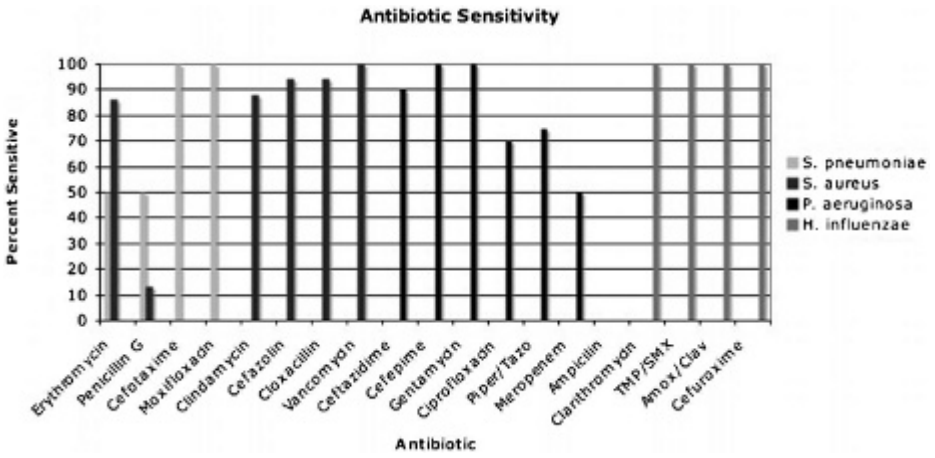

Figure 2. Sensitivity profiles of *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Moraxella catarrhalis*, and *Pseudomonas aeruginosa* isolated. TMP-SMX = trimethoprim-sulfamethoxazole.

that heavy growth of *S. aureus* represented a true pathogen, whereas light growth represented a commensal isolate. In our study, moderate to heavy growth of *S. aureus* was seen in 75% of the isolates, suggesting its role as a true pathogen in this setting.

Our study isolated gram-negative bacteria in 42% of isolates, with *H. influenzae* (16%) and *M. catarrhalis* (7%) being the most prevalent (see Figure 1). This is in keeping with the published literature (34.1%).[18] There is significant evidence for the pathogenic role that gram-negative bacteria (particularly *Prevotella*, *Fusobacterium*, and *Peptostreptococcus* sp) play in chronic sinonasal disease.[19] Our study supports the recognition of gram-negative bacteria as an important organism in patients presenting to a tertiary sinus centre.

The majority of *S. aureus* isolates found in the study were resistant to penicillin G, and between 6 and 14% were resistant to clindamycin, cefazolin, erythromycin, and cloxacillin (see Figure 3). Three cases of MRSA were identified, one in a patient with cystic fibrosis. This corresponded to an incidence of MRSA in 2% of total isolates. The incidence of MRSA identified in this study appears to be much lower than that in nonrhinologic cohorts[21] but similar to international data in patients with sinonasal disease.[3] In this context, the resistance patterns show that first-generation cephalosporins likely represent the most effective antimicrobial agents for *S. aureus* infections.

With the exception of erythromycin and penicillin G, *S. pneumoniae* showed sensitivity to all of the antimicrobials tested (see Figure 2). *P. aeruginosa* organisms showed

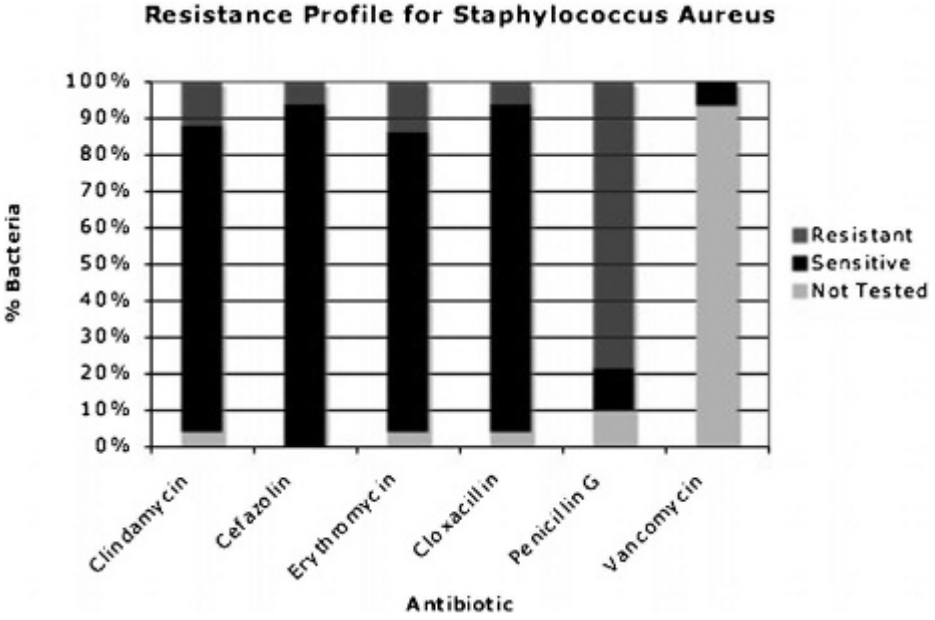

Figure 3. Resistance profiles of *Staphylococcus aureus* isolated.

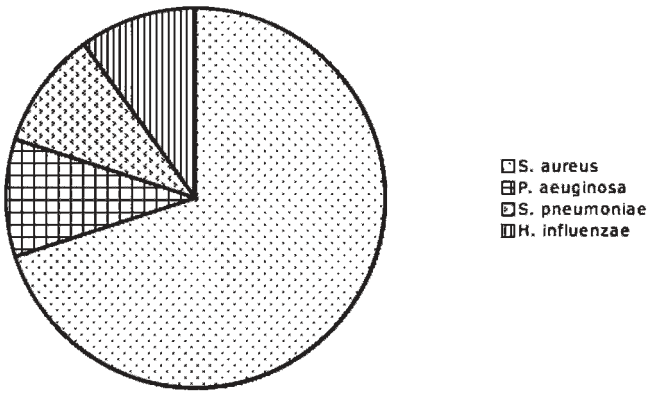

Figure 4. Recurrent bacterial organisms in patients who require repeat sinus culture.

variable resistance patterns, with many organisms being resistant to tobramycin, ciprofloxacin, and TMP-SMX (see Figure 2), with ceftazidime representing the best choice of antibiotic. All the *M. catarrhalis*–positive isolates tested showed resistance to ampicillin (see Figure 2). Several studies have linked this phenomenon to the high incidence ($>$ 90%) of β-lactamase producing strains of *M. catarrhalis*.[22,23] All other antimicrobials tested, which included clarithromycin, cefuroxime, ceftazidime, TMP-SMX, and amoxicillin–clavulanic acid, had favourable sensitivity profiles toward *M. catarrhalis*. In our study, two *H. influenzae* isolates showed resistance to ampicillin, one of which also showed concomitant resistance to TMP-SMX. The development of multidrug-resistant strains of *H. influenzae* to both ampicillin and TMP-SMX has been demonstrated in the international literature to occur at an incidence of 39.3%.[24]

In the era of antimicrobial resistance, clinicians are continually faced with the challenge of how best to eradicate bacteria from the sinuses. Historically, the use of a broad-spectrum antibiotic for a period of 4 to 6 weeks was considered the standard of practice.[8,9] As demonstrated in this study, certain traditional antimicrobial agents that were once effective no longer provide adequate coverage for all bacterial strains. Therefore, increased consideration must be made as to the most appropriate antimicrobial agent and course of therapy when treating chronic sinonasal disease.

To date, uncertainty exists as to the best antimicrobial course in chronic sinonasal disease. With the use of non–culture-directed broad-spectrum antibiotics coming under heavy scrutiny, the practice of culture-directed therapy is now becoming the gold standard[1] for the management of sinonasal disease. In this study, antimicrobial management was culture directed. Patient samples were collected in a sterile manner under endoscopic guidance at the time of the visit and cultured by the hospital laboratory in accordance with the NCCLS guideline[12,13] to determine antimicrobial sensitivity.

The use of culture-directed therapy has made a direct impact on the low incidence of MRSA seen in our study. Similarly, Bhattacharyya and Kepnes, looking at antimicrobial resistance trends over a 7-year period, attributed the low and nonescalating incidence of MRSA to their use of culture-directed antimicrobial therapy.[9] At our institution, careful collection of swabs proves vital for ensuring accurate identification of bacterial organisms. When a nasal swab is used, direct contact with purulence for at least 10 seconds has become standard of care. We encourage diligent specimen collection in combination with culture-directed therapy in an effort to minimize antimicrobial resistance. Similarly, we caution the use of broad-spectrum antibiotics in the setting of chronic sinonasal disease.

Table 2 provides a breakdown of recommended antimicrobial agents based on antimicrobial sensitivity profiles determined in this study. A first-generation cephalosporin such as cefazolin appears to be the best choice for *S. aureus* infections, whereas moxifloxacin for *S. pneumoniae* and gentamicin topically for *Pseudomonas* were the most efficacious antibiotics.

There are several limitations to this study. One limitation includes the retrospective nature of this study's design. In addition, despite all precautions, contamination of the collection apparatus owing to its passage through

Table 2. Antimicrobial Recommendations Based on Antimicrobial Sensitivity Profile

Bacteria	*Therapy of Choice*	*% Resistance*
Staphylococcus aureus	Cefazolin	6
	Clindamycin	12
	Erythromycin	14
Streptococcus pneumoniae	Moxifloxacin	0
Moraxella catarrhalis	Clarithromycin	0
	Trimethoprim-sulfamethoxazole	0
	Amoxicillin–clavulanic acid	0
Haemophilus influenzae	Ampicillin	10
Pseudomonas aeruginosa	Ceftazidime	10
	Gentamicin	0

the nasal vestibule could have occurred when collecting sinus specimens. We have taken precautions to reduce contamination by collecting all samples under endoscopic guidance. Unfortunately, this study did not identify specific antibiotics prescribed or previous operative interventions. A future prospective study with documentation of antibacterial use and previous operative interventions would be of great benefit in making further recommendations.

Conclusion

MRSA does not appear to pose a significant risk of morbidity in our patient population. However, ongoing concerns regarding the increasing prevalence of *S. aureus* and gram-negative bacteria in chronic sinonasal disease highlight the importance of using culture-directed antimicrobial therapy with the goal of minimizing future resistance patterns.

Acknowledgement

Financial disclosure of authors and reviewers: None reported.

References

1. Kingdom TT, Swain RE Jr. The microbiology and antimicrobial resistance patterns in chronic rhinosinusitis. Am J Otolaryngol 2004;25:323–8, doi:10.1016/j.amjoto.2004.03.003.
2. Fokkens WJ, Lund VJ, Mullol J, et al. European position paper on rhinosinusitis and nasal polyps. Rhinol Suppl 2007;20:1–136.
3. Philpott CM, Sharma A, McKiernan DC. Does methicillin-resistant Staphylococcus aureus have a significant role in the peri-operative course of patients undergoing rhinological surgery? J Laryngol Otol 2009;123:191–4, doi:10.1017/S0022215108002855.
4. Sharma A, Philpott C, Pope L, McKiernan D. Methicillin resistant Staphylococcus aureus: is it a problem for nasal surgery? J Laryngol Otol 2007;121:415–8.
5. Mangram AJ, Horan TC, Pearson ML, et. al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 1999;20:250–78, doi:10.1086/501620.
6. Nadel DM, Lanza DC, Kennedy DW. Endoscopically guided cultures in chronic sinusitis. Am J Rhinol 1998;12:233–41, doi:10.2500/105065898781390000.
7. Wegner DL. No mercy for MRSA: treatment alternatives to vancomycin and linezolid. MLO Med Lab Obs 2005;37:26–9.
8. Benninger MS, Anon J, Mabry RL. The medical management of rhinosinusitis. Otolaryngol Head Neck Surg 1997;117 (3 Pt 2):S41–9, doi:10.1016/S0194-5998(97)70006-8.
9. Bhattacharyya N, Kepnes LJ. The risk of development of antimicrobial resistance in individual patients with chronic rhinosinusitis. Arch Otolaryngol Head Neck Surg 2004;130:1201–4, doi:10.1001/archotol.130.10.1201.
10. Lin A, Busaba NY. Staphylococcus aureus and endoscopic sinus surgery. Curr Opin Otolaryngol Head Neck Surg 2006;14:19–22, doi:10.1097/01.moo.0000193172.69697.08.
11. Murray PR, editor. Manual of clinical microbiology. 7th ed. Washington (DC): ASM Press; 1999.
12. National Committee for Clinical Laboratory Standards. Methods for Dilution antimicrobial susceptibility tests for bacteria that grow aerobically. Approved Standard M7-A5. Wayne (PA): National Committee for Clinical Laboratory Standards; 2000.
13. National Committee for Clinical Laboratory Standards. Performancy standards for antimicrobial disk susceptibility tests. Approved Standard M2-A7. Wayne (PA): National Committee for Clinical Laboratory Standards; 2000.
14. Hsu J, Lanza DC, Kennedy DW. Antimicrobial resistance in bacterial chronic sinusitis. Am J Rhinol 1998;12:243–8, doi:10.2500/105065898781390055.
15. Manarey CR, Anand VK, Huang C. Incidence of methicillin-resistant Staphylococcus aureus causing chronic rhinosinusitis. Laryngoscope 2004;114:939–41, doi:10.1097/00005537-200405000-00029.
16. Biel MA, Brown CA, Levinson RM, et al. Evaluation of the microbiology of chronic maxillary sinusitis. Ann Otol Rhinol Laryngol 1998;107:942–5.
17. Doyle PW, Woodham JD. Evaluation of the microbiology of chronic ethmoid sinusitis. J Clin Microbiol 1991;29:2396–400.
18. Bolger WE. Gram negative sinusitis: an emerging clinical entity. Am J Rhinol 1994;8:279–84, doi:10.2500/105065894781874205.
19. Brook I. The role of bacteria in chronic rhinosinusitis. Otolaryngol Clin North Am 2005;38:1171–92, doi:10.1016/j.otc.2005.08.007.
20. Brook I, Foote PA, Hausfeld JN. Increase in the frequency of recovery of methicillin-resistant Staphylococcus aureus in acute and chronic maxillary sinusitis. J Med Microbiol 2008;57:1015–7, doi:10.1099/jmm.0.2008/000851-0.
21. Deresinski S. Methicillin-resistant Staphylococcus aureus: an evolutionary, epidemiologic, and therapeutic odyssey. Clin Infect Dis 2005;40:562–73, doi:10.1086/427701.
22. Thornsberry C, Sahm DF. Resistance of respiratory tract pathogens: an international study 1997-1998. J Chem 2000;12 Suppl 4:16–27.
23. Fung CP, Powell M, Seymour A, et al. The antimicrobial susceptibility of *Moraxella catarrhalis* isolated in England and Scotland in 1991. J Antimicrob Chemother 1992;30:47–55, doi:10.1093/jac/30.1.47.
24. Gur D, Ozalp M, Sumerkan B, et al. The prevalence of antimicrobial resistance in *Haemophilus influenzae, Streptococcus pneumoniae, Moxaella catarrhalis* and *Streptococcus pyogenes*: results of a multicentre study in Turkey. Int J Antimicron Agents 2002;19:207–11, doi:10.1016/S0924-8579(02)00003-1.