

Microbiology of chronic rhinosinusitis

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Abstract Most sinus infections are viral and only a small percentage develop bacterial infection. Rhino-, influenza, and para-influenza viruses are the most frequent viral causes of sinusitis. The most common bacterial isolates from children and adult patients with community-acquired acute bacterial sinusitis are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Moraxella catarrhalis*, and *Streptococcus pyogenes*. *Staphylococcus aureus* and anaerobic organisms (*Prevotella* and *Porphyromonas*, *Fusobacterium*, and *Peptostreptococcus* spp.) are the commonest isolates in chronic rhinosinusitis (CRS). Aerobic and anaerobic beta lactamase-producing bacteria (BLPB) were recovered from over a third of these patients. Methicillin-resistant *S. aureus* (MRSA) accounted for over 60 % of *S. aureus* isolates. *Pseudomonas aeruginosa* and other aerobic and facultative Gram-negative rods are frequently recovered in nosocomial sinusitis, the immunocompromised host, individuals with human immunodeficiency virus infection, and in cystic fibrosis. The CRS infection evolves the formation of a biofilm that might play a significant role in the pathogenesis and persistence of CRS. The microbiology of sinusitis is influenced by previous antimicrobial therapy, vaccinations, and the presence of normal flora capable of interfering with the growth of pathogens. Recognition of the unique microbiology of CRS and their antimicrobial susceptibility is of great importance when selecting antimicrobial therapy.

Introduction

The upper respiratory tract, including the nasopharynx, is colonized by normal bacterial flora that includes potential pathogens capable of causing respiratory tract infections, including sinusitis [1]. These potential pathogens can spread from the nasopharynx into the sinus cavity during viral respiratory infection and cause sinus infection [2].

The dynamic of many upper respiratory tract infections, including sinusitis, can evolve through several stages. The early phase is viral, which usually lasts up to 10 days and ends with complete recovery in most individuals [3]. However, some individuals (estimated at 0.5 %) develop an acute bacterial infection generally caused by facultative aerobic bacteria (e.g., *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis*). If the acute infection does not resolve, anaerobic bacteria that originate from the oral flora can become the predominate pathogens. These phases were demonstrated in patients with maxillary sinusitis by performing serial culture throughout their infection [4]. The microbiology of sinusitis is influenced by previous antimicrobial therapy, vaccinations, and the presence of normal flora capable of interfering with the growth of pathogens [5].

Chronic rhinosinusitis (CRS) is a prevalent multifactorial disease process in which bacteria are believed to play a role in the propagation of inflammation. Recognition of the unique microbiology of CRS is of great importance when selecting the antimicrobial therapy for this condition. This review presents the microbiology of all chronic forms of sinusitis.

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Bacteriology of chronic rhinosinusitis

Although the exact etiology of the inflammation associated with CRS is uncertain, the presence of bacteria within

the sinuses has been well documented [6, 7]. It is plausible that, in chronic sinusitis, mucociliary clearance and host defenses are impaired to the point that the sinus cavity loses its normal sterility and becomes colonized with nasal flora. Thus, chronic sinusitis may not truly be an “infectious process” but an aberration of the normal anatomy responsible for drainage and damage to the mucosa of the sinus cavity. Most clinicians believe that microorganisms play a major role in the etiology and pathogenesis of most cases of CRS and prescribe antimicrobial therapy. In contrast to the agreement regarding the microbiology of acute sinusitis, there is disagreement regarding the microbiology of CRS. Unfortunately, there are several issues that confound the reliability of many of microbiological studies and, therefore, contribute to the disparity of their results. These issues include: various methods used to sample the sinus cavity; failure to sterilize the area through which the trocar or endoscope is passed; different sinuses or areas that are sampled (i.e., ethmoid bulla or maxillary antrum or middle meatus); lack of assessment of the inflammatory response; lack of quantitation of bacteria; previous or current use of antibiotics; variable patient selection (i.e., age, duration, extent of disease, surgical or non-surgical subjects); presence of nasal polyps; and time of culture transport and method of culture.

The CRS infection involves the formation of a biofilm that might play a significant role in the pathogenesis and persistence of CRS [8]. This is three-dimensionally structured, by adherent microorganisms surrounded by an extracellular polymeric substance. The biofilm is polymicrobial, providing the organisms numerous advantages, such as passive resistance, synergistic metabolic cooperation, by-product influence, shielding of beta-lactam susceptible organisms by beta-lactamase-producing ones, quorum sensing systems, an enlarged gene pool with more efficient DNA, sharing, and many other synergies, which give them a competitive advantage. In general, the higher the diversity, the more robust the biofilm is in terms of its survivability [9].

Bacterial diversity and composition are predictors of the surgical outcome of CRS. Only two conditions (presence of purulence and comorbid condition of asthma) were associated with significant alterations in microbial community composition [10] in 27 patients with CRS who were followed postoperatively. Those with better outcomes had more diverse bacterial communities present.

There are significant differences in the microbiology of CRS as compared with acute one (Table 1). *Staphylococcus aureus*, *Staphylococcus epidermidis*, and anaerobic Gram-negative bacteria predominate in CRS. The true prevalence of anaerobic bacteria in CRS is inaccurate in studies that did not use methods adequate for their recovery. The pathogenicity of some of the low virulence bacteria, such as *S.*

epidermidis, a colonizer of the nasal cavity, is questionable [15]. The lack of quantitation in most studies prevents an assessment of both the density of organisms and the accompaniment of an inflammatory response. The frequent recovery of *S. epidermidis* from swabs obtained from the middle meatus of normal subjects suggests that they are likely contaminants. However, in the presence of a large number of white blood cells and organisms (on Gram stain) and a heavy growth of only *S. epidermidis*, the possibility of a true infection by this organism should be entertained [16–19].

Recovery of Gram-negative enteric rods, including *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Proteus mirabilis*, *Enterobacter* spp., and *Escherichia coli*, was also reported [17–19]. Since these bacteria are rarely recovered from middle meatus cultures obtained from healthy individuals, their isolation from symptomatic patients suggests their pathogenic role. These organisms might have been selected out in these individuals following the administration of antimicrobial therapy.

The exact chain of events leading to CRS has been hard to identify or prove [20]. It has been suggested that CRS is an extension of unresolved acute sinusitis. Viral acute sinusitis can establish conditions supportive of the growth of aerobic and anaerobic bacteria [21].

The persistence of the infection can foster the growth of anaerobic bacteria. The shift of the microbiology from an initial viral infection to aerobic to anaerobic bacterial growth can occur as the inflammation persists.

The transition from acute to CRS was evaluated by repeated endoscopic sinus aspirations in five patients [4]. Most organisms found in the first cultures were aerobic or facultatives: *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*. Failure to respond to therapy was associated with the appearance of resistant bacteria in subsequent aspirates. These included *Fusobacterium nucleatum*, *Prevotella*, *Porphyromonas*, and *Peptostreptococcus* spp. Improvement in the patients' condition occurred following the administration of appropriate antimicrobials and, in three patients, also by surgical drainage.

This study shows that the aerobic and facultative isolates are gradually replaced by anaerobic ones [4]. This transition may be the result of selective pressure of antimicrobials that enable resistant bacteria to survive, as well as due to the development of conditions appropriate for anaerobic bacterial growth, which include the reduction in oxygen tension and an increase in acidity within the sinus cavity. These changes are created by the persistent edema and swelling, which reduce blood supply, and by the utilization of oxygen by the aerobic bacteria [22]. The emergence of anaerobes that possess virulence factors such as a capsule can also play a role [23].

Studies that used adequate methods for the recovery of anaerobic bacteria found these organisms in more than half of the cases, whereas the pathogens in acute sinusitis (e.g., *S.*

Table 1 Percentage of recovery of organisms from chronic sinusitis in adults [11–14]

Bacteria	Maxillary sinus (n = 66)	Ethmoid sinus (n = 17)	Frontal sinus (n = 13)	Sphenoid sinus (n = 7)
Aerobic bacteria				
<i>S. aureus</i>	14	24	15	14
<i>S. pyogenes</i>	8	6	–	–
<i>S. pneumoniae</i>	6	6	–	–
<i>H. influenzae</i>	5	6	15	14
<i>M. catarrhalis</i>	6	–	–	–
Enterobacteriaceae	6	47	8	28
<i>P. aeruginosa</i>	3	6	8	14
Anaerobic bacteria				
<i>Peptostreptococcus</i> spp.	56	59	38	57
<i>P. acnes</i>	29	18	8	29
<i>Fusobacterium</i> spp.	17	47	31	54
<i>Prevotella</i> and <i>Porphyromonas</i>	47	82	62	86
<i>B. fragilis</i>	6	–	15	–

Since some patients had multiple isolates from the same specimen, the sum of percentages in each column exceeds 100 %

pneumoniae, *H. influenzae*, *M. catarrhalis*) are found in lower frequency [11, 24–27].

CRS is often a polymicrobial synergistic infection [23] and may, therefore, be harder to eradicate with narrow-spectrum antimicrobials. CRS caused by anaerobes is of particular concern because many of the infection's complications (e.g., mucocele formation, osteomyelitis, local and intracranial abscess) are caused by these bacteria [28].

The role of anaerobes in CRS is supported by several studies. Intranasal inoculation of *Bacteroides fragilis* to rabbits induces CRS associated with rapid emergence of IgG antibodies against this organism [29]. Antibodies (IgG) against two anaerobic organisms commonly recovered from sinus aspirates (*Fusobacterium nucleatum* and *Prevotella intermedia*) were detected in individuals with CRS [30]. Antibody levels decreased in patients who responded to antimicrobial therapy, but remained elevated in those who failed treatment.

Recent studies employing molecular culture (bacterial tag-encoded FLX amplicon pyrosequencing [bTEFAP]) found that anaerobic species predominated, while *S. aureus* was detected in half of the specimens [31, 32]. A study using sequencing of the species-specific 16S ribosomal DNA fragment for the genetic identification of bacteria illustrated the recovery of anaerobes in half of the 18 patients with CRS [31]. Ramakrishnan et al. [10], using the same methodology, found that purulence in CRS was associated with significant expansions of Bacteroidetes and fusobacteria species.

A summary of 20 studies that also evaluated the role of anaerobes in CRS carried out since 1974, including 2006 patients (373 were children) is shown in Table 2 [26, 27, 33–50]. Anaerobes were recovered in 8 to 93 % of the patients. The

differences in isolation rates may be due to differences in the methodologies used for the transportation and cultivation of specimens, patient population, location, and previous antimicrobial treatment.

Studies in children

There have been 12 studies of the microbiology of CRS in children since 1981 [26, 41, 44, 48–57]. Four of these studies were prospective [44, 51, 52, 56] and seven were retrospective. In all but four studies, the maxillary sinus was sampled by transnasal aspiration. The most common criteria for evaluation were symptoms that lasted over 90 days. An attempt was made to sterilize the nose prior to obtaining the culture only in five studies and bacterial quantitation was rarely done. In two of the studies, members of the normal nasal flora isolates were the most common organisms recovered. It is difficult to assign pathologic significance to these organisms. In the remaining studies, the pathogens common in acute infection were recovered in about 60 % of cases (i.e., *H. influenzae*, *S. pneumoniae*, and *M. catarrhalis*). This was especially true when the criteria for entry included purulent secretions. In the remaining 30–40 % of children, contaminants were recovered. Anaerobes were recovered in six studies (Table 2), the only ones that employed methods for their recovery [26, 41, 44, 48, 51].

Staphylococcus aureus (19 %) and alpha-hemolytic streptococci (23 %) were the commonest isolates in ethmoid sinusitis in one study [54], and *S. epidermidis* and alpha-hemolytic streptococci in another [52]. *Moraxella catarrhalis* was the

Table 2 Summary of 20 studies that evaluated the role of anaerobic bacteria in chronic rhinosinusitis (CRS)

Reference	No. of patients	Condition	Percentage of patients from which anaerobic organisms were isolated	Percentage of anaerobic bacteria/total number of organisms
Frederick and Braude [33]	83 adults	Chronic sinusitis	75	52
Van Cauwenberge et al. [34]	66 adults	Acute and chronic sinusitis	39	39
Karma et al. [35]	40 adults	Chronic sinusitis	100	19
Berg et al. [36]	54 adults	Chronic sinusitis	33	42
Fiscalla and Chow [37]	15 adults	Chronic sinusitis	38	48
Sedallian et al. [38]	40, ages not given	Chronic sinusitis	69	46
Simoncelli et al. [39]	132 adults	Chronic sinusitis	NS	22
Tabaqchali [40]	35, ages not given	Chronic sinusitis	70	39
Brook and Yocum [41]	40 children	Chronic sinusitis	100	80
Hartog et al. [42]	90 adults	Chronic sinusitis	81	29
Ito et al. [43]	10, ages not given	Chronic maxillary sinusitis	100	60
Erkan et al. [44]	93 children	Chronic maxillary sinusitis	93	93
Erkan et al. [45]	126 adults	Chronic maxillary sinusitis	90	88
Brook et al. [26]	68 adults	Chronic maxillary sinusitis	100	82
Edelstein et al. [46]	114 adults	Acute and chronic sinusitis	NS	12
Klossek et al. [47]	412	Chronic sinusitis	NS	26
Finegold et al. [27]	150 adults	Chronic maxillary sinusitis	54	49
Hsin et al. [48]	165 children	Chronic maxillary sinusitis	32	8
Goldenhersh et al. [49]	12 children	Chronic maxillary sinusitis	8	5
Stokken et al. [50]	41 children	Chronic maxillary sinusitis	NS	37
Brook et al.	32 children	Chronic maxillary sinusitis	53	42

most frequent isolate in a study of children with allergies, although 25 % of them had polymicrobial flora [49].

Brook and Yocum [41] evaluated 40 children with CRS. The involved sinuses were the maxillary (15 cases), ethmoid (13), and frontal (7). Pansinusitis was diagnosed in five children. A total of 121 isolates (97 anaerobic and 24 aerobic) were isolated. Anaerobes were detected in all 37 culture-positive specimens, and in 14 instances (38 %), they were mixed with aerobes. The predominant anaerobes were Gram-negative bacilli (36), anaerobic Gram-positive cocci (28), and *Fusobacterium* spp. (13). The predominant aerobic bacteria were alpha-hemolytic streptococci (7), *S. aureus* (7), and *Haemophilus* spp. (4).

Brook et al. [51] correlated the organisms isolated in concurrent chronic otitis media with effusion and chronic maxillary sinusitis in 32 children. Two-thirds of the children had a bacterial etiology. The most common isolates were *H. influenzae* (9 isolates), *S. pneumoniae* (7), *Prevotella* spp. (8), and *Peptostreptococcus* spp. (6). Microbiological concordance between the ear and sinus was found in 22 (69 %) culture-positive children.

Erkan et al. [44] studied 93 chronically inflamed maxillary sinuses. Anaerobic bacteria were recovered in 81 of 87 (93 %) culture-positive specimens and were isolated alone in 61 (70 %) and mixed with aerobic or facultative bacteria in 20

(23 %). Aerobic or facultative bacteria were found alone in six instances (7 %). A total of 261 isolates, 19 anaerobes, and 69 aerobes or facultatives were found. The predominant anaerobes were *Bacteroides* spp. and anaerobic cocci; the main aerobes or facultatives were *Streptococcus* spp. and *S. aureus*.

Hsin et al. [48] obtained cultures from 165 children with CRS. Of the 399 isolates, 21 % were alpha-hemolytic streptococci, 19 % *H. influenzae*, 14 % *S. pneumoniae*, 9 % *S. aureus*, and 8 % anaerobes. A significant increase in the antimicrobial resistance of the aerobic bacteria over the 6-year study period was noted.

Stokken et al. [50] recovered pathogenic organisms from 21 of 41 (51 %) patients with CRS. The predominant microorganisms included anaerobic bacteria (16 isolates), *S. aureus* (8), and *S. pneumoniae* (4). The authors did not identify half of the anaerobic isolates and did not identify organisms in polymicrobial infections.

Studies in adults

The presence of anaerobic bacteria in CRS in adults is often clinically significant [58, 59]. Finegold et al. [27] found that recurrences of signs or symptoms of bacterial maxillary sinusitis associated with anaerobes were twice as frequent as those

associated with aerobes when counts of anaerobes were above 10^3 colony-forming units per milliliter.

Anaerobes were frequently recovered whenever appropriate techniques for their cultivation were employed. The predominant ones were pigmented *Prevotella*, *Fusobacterium*, and *Peptostreptococcus* spp. The most common aerobes were *S. aureus*, *M. catarrhalis*, and *Haemophilus* spp. Aerobic and anaerobic beta-lactamase-producing bacteria (BLPB) were recovered from over a third of these patients [11, 17, 24, 25]. These BLPB were *S. aureus*, *Haemophilus*, *Prevotella*, *Porphyromonas*, and *Fusobacterium* spp. Unfortunately, the levels of resistance to other antimicrobials in the microbial flora recovered in chronic sinusitis was not evaluated in other studies.

Brook and Frazier [60] correlated the microbiology with the history of sinus surgery in 108 individuals with chronic maxillary sinusitis and noted a higher rate of recovery of *P. aeruginosa* and other Gram-negative bacilli in those who had previous sinus surgery. Anaerobes were, however, recovered significantly more often in those who had not had prior surgery.

Cleland et al. [61] retrospectively studied the aerobic bacteriology of CRS in 513 patients who had a surgical revision of their sinuses. Organisms were recovered in 83 % of patients, and the average number of isolates/patient was 0.95. The predominate organisms were *S. aureus* (35 % of patients), *P. aeruginosa* (9 %), *Haemophilus* spp. (7 %), and *S. pneumoniae* (5 %). Revision patients were more likely to grow *S. aureus* ($p=0.001$), *P. aeruginosa* ($p=0.044$), and have a positive culture ($p=0.001$). Asthma was correlated with a positive culture ($p=0.039$). No difference was determined between polyp and non-polyp patients for any of the bacterial outcomes.

Brook evaluated the microbiology of 13 chronically infected frontal [12], seven sphenoid [13], and 17 ethmoid sinuses [14] (Table 1). Anaerobic bacteria were recovered in over two-thirds of the patients. The predominant ones were *Prevotella*, *Peptostreptococcus*, and *Fusobacterium* spp. The most common aerobes were Gram-negative bacilli (*H. influenzae*, *K. pneumoniae*, *E. coli*, and *P. aeruginosa*).

Brook et al. [62] compared the rate of recovery of methicillin-resistant *S. aureus* (MRSA) between the periods 2001–2003 and 2004–2006 in chronic maxillary sinusitis. Cultures were obtained from 214 patients with chronic maxillary sinusitis; 97 isolates were recovered in the 2 years between 2001 and 2003, and 117 in the 2 years between 2004 and 2006. *Staphylococcus aureus* was found in 15 (15 %) of the patients with chronic sinusitis between 2001 and 2003, four (27 %) of which were MRSA, and from 23 (20 %) of the patients with chronic sinusitis between 2004 and 2006, 14 (61 %) of which were MRSA ($p<0.05$). Antimicrobial therapy was administered over the last 3 months to 122 (57 %) of the patients with chronic sinusitis. MRSA was isolated more

often from these individuals (28/122; 23 %) than from those not treated previously (10/92 or 11 %) ($p<0.05$).

Nadel et al. [17] also found Gram-negative rods more often in patients who had previous sinus surgery or irrigation. *Pseudomonas aeruginosa* was also more common in those who received systemic steroids. Other studies have also noted a shift to Gram-negative organisms in individuals who have been repeatedly treated [16, 19, 62]. Their bacterial isolates include *Pseudomonas* spp., *Enterobacter* spp., MRSA, *H. influenzae*, and *M. catarrhalis*.

Ramakrishnan et al. [10] examined the resident microbiota of CRS subtypes and determined whether bacterial diversity is a predictor of disease outcomes. The presence of purulence in CRS was associated with expansion of *Prevotella* ($p=0.07$), *Streptococcus* ($p=0.05$), *Veillonella* ($p=0.04$), and *Leptotrichia* ($p=0.09$) species, along with decreased members of the genera *Propionibacterium* ($p=0.02$), *Anaerococcus* ($p=0.03$), *Pseudomonas* ($p=0.01$), *Ralstonia* ($p=0.02$), and *Stenotrophomonas* ($p=0.03$) species.

Bacteriology of chronic maxillary sinusitis associated with nasal polyposis

Nasal polyps can impair paranasal sinus ventilation and drainage by blocking the ostiomeatal complex. Several studies that did not employ adequate methods for the recovery of anaerobes did not recover any organisms or only a few [63].

Brook and Frazier studied sinus aspirates from 48 chronically inflamed maxillary sinuses from patients who had nasal polyposis [64]. Bacterial growth was present in 46 (96 %) specimens. Aerobic or facultatives were isolated in 6 (13 %) specimens, anaerobes alone in 18 (39 %), and mixed aerobic and anaerobic bacteria in 22 (48 %). There were 110 bacterial isolates (2.4 per specimen); 39 were aerobic or facultative (0.85 per specimen). The predominant aerobic or facultative isolates were: *S. aureus*, microaerophilic streptococci, *H. influenzae*, and *M. catarrhalis*. There were 71 anaerobes recovered (1.5 per specimen); the predominant ones were *Peptostreptococcus* spp., *Prevotella* spp., *Porphyromonas asaccharolytica*, *Fusobacterium* spp., and *Propionibacterium acnes*.

Kim et al. [65] studied the microbiology and antimicrobial susceptibility of maxillary sinus aspirates in CRS with nasal polyps in 81 patients. Aerobes were isolated from 48 % of the aspirates and included *S. aureus*, *H. influenzae*, and *S. pneumoniae*. Anaerobes were recovered from 18.5 % and the predominant ones were *Prevotella* and *Peptostreptococcus* spp.

Ramakrishnan et al. [10], utilizing molecular phylogenetic analysis of 16S rDNA pyrosequences methodology, found that the presence of nasal polyps was not independently associated with general bacterial community alterations. Liu et al.

[66] compared the endoscopically obtained bacteriologic profiles in the middle meatus of 165 patients with CRS with nasal polyps (CRSwNP) with 76 patients with CRS without nasal polyps (CRSSNP) and 44 control subjects. Aerobic and facultative anaerobic bacteria were detected in the samples from all three study groups, of which the most common aerobic bacteria were coagulase-negative staphylococci, *Corynebacterium* spp., *S. aureus*, and *H. influenzae*. In contrast, few anaerobic bacteria were isolated from the three study groups, suggesting the utilization of inadequate methods for their recovery. In CRSwNP patients, significantly more Gram-negative aerobic and facultative anaerobic bacteria were isolated from the subgroup with normal eosinophil numbers than from the subgroup with increased blood eosinophils ($p=0.005$). *Staphylococcus aureus* and *Streptococcus*, *Haemophilus*, *Enterobacter*, and *Corynebacterium* spp. were associated with CRSwNP patients. The isolation of equally high numbers of coagulase-negative staphylococci in all three groups suggests that the specimens were contaminated with skin flora.

These findings suggest that the microbiology of chronic maxillary sinuses with polyposis is polymicrobial aerobic–anaerobic and is not different from those who develop CRS without this condition.

Bacteriology of acute exacerbation of CRS

Acute exacerbation of CRS (AECS) is defined as a sudden worsening of the baseline CRS with either worsening or new symptoms. Typically, the acute (not chronic) symptoms resolve completely between exacerbations [67]. Brook et al. evaluated the bacteriology of acute AECS [68] by performing repeated endoscopic sinus aspirates in seven patients over a period of 125 to 242 days. Microorganisms were found in all 22 aspirates and the number of isolates varied between 2 and 4. A total of 54 isolates were recovered, 16 aerobic and facultatives and 38 anaerobic. The aerobes were seven *H. influenzae*, three *S. pneumoniae*, three *M. catarrhalis*, two *S. aureus*, and one *K. pneumoniae*. The anaerobes included pigmented *Prevotella* and *Porphyromonas* (19), *Peptostreptococcus* (9), and *Fusobacterium* spp. (8) and *P. acnes* (2). A change in the types of isolates occurred in all consecutive cultures obtained from the same patients, as different organisms emerged, and previously cultured isolates were no longer present. An increase in antimicrobial resistance was found in six instances. These findings demonstrate the microbial dynamics of AECS, where anaerobic and aerobic bacteria prevail, and highlight the importance of obtaining cultures from individuals with this infection that can guide the selection of proper antimicrobial therapy.

Brook [69] compared the aerobic and anaerobic microbiology of maxillary AECS with the microbiology of chronic maxillary sinusitis. Included in the study were 32 patients with CRS and 30 with AECS. A total of 81 isolates were recovered

from the 32 cases (2.5 per specimen) with CRS: 33 aerobic and 48 anaerobic. Aerobes alone were recovered in eight specimens (25 %), anaerobes only were isolated in 11 (34 %), and mixed aerobes and anaerobes were recovered in 13 (41 %). The predominant aerobic and facultative were Enterobacteriaceae and *S. aureus*. The predominant anaerobes were *Peptostreptococcus* spp., *Fusobacterium* spp., anaerobic Gram-negative bacilli, and *P. acnes*. A total of 89 isolates were recovered from the 30 cases (3.0 per specimen) with AECS: 40 aerobic and facultatives and 49 anaerobic. Aerobes were recovered in eight instances (27 %), anaerobes only in 11 (37 %), and mixed aerobes and anaerobes were recovered in 11 (37 %). The predominant aerobes were *S. pneumoniae*, Enterobacteriaceae, and *S. aureus*. The commonest anaerobes were *Peptostreptococcus* spp., *Fusobacterium* spp., anaerobic Gram-negative bacilli, and *P. acnes*. This study illustrates that the organisms isolated from patients with AECS were predominantly anaerobic and were similar to those generally recovered in CRS. However, aerobic bacteria that are usually found in acute infections (e.g., *S. pneumoniae*, *H. influenzae*, and *M. catarrhalis*) can also emerge in some of the episodes of AECS.

Bacteriology of nosocomial sinusitis

Individuals with nosocomial sinusitis are usually those who require extended periods of intensive care (postoperative patients, burn victims, patients with severe trauma) involving prolonged endotracheal or nasogastric intubation [70]. Patients with prolonged nasotracheal intubation are at a higher risk for nosocomial sinusitis than those with orotracheal intubation [71]. About a quarter of patients requiring nasotracheal intubation for more than 5 days develop nosocomial sinusitis [72]. The usual pathogens are Gram-negative enteric bacteria (e.g., *P. aeruginosa*, *K. pneumoniae*, *Enterobacter* spp., *P. mirabilis*, *Serratia marcescens*) and Gram-positive cocci aerobic (streptococci and staphylococci) [70–75]. However, it is unclear if these isolates are true pathogens or environmental colonizers.

Souweine et al. [76] studied the microbiology of ventilator-associated maxillary sinusitis in 24 patients. Nine cultures yielded a single bacteria and 15 were polymicrobial. An average of two organisms per sinus was recovered; 21 Gram-positive and 22 Gram-negative bacteria, and five yeasts. *Pseudomonas aeruginosa* and enterococci were the most commonly identified organisms.

Brook and Shah evaluated the microbiology of nosocomial sinusitis in nine neurologically impaired children. Anaerobic bacteria, always mixed with aerobic and facultative bacteria, were present in 6 (67 %) and aerobic bacteria only were found in 3 (33 %) [77]. There were 24 bacterial isolates: 12 aerobic or facultative and 12 anaerobic. The predominant aerobes

were *K. pneumoniae*, , and *S. aureus* (two each) and *P. mirabilis*, *P. aeruginosa*, *H. influenzae*, *M. catarrhalis*, and *S. pneumoniae* (one each). The predominant anaerobes were *Prevotella* spp. (5), *Peptostreptococcus* spp. (4), *F. nucleatum* (2), and *B. fragilis* (1). Organisms similar to those recovered from the sinuses were also found in the tracheostomy site and gastrostomy wound aspirates in five of seven instances. This study demonstrates the unique microbiology of nosocomial sinusitis in neurologically impaired children, where facultative and anaerobic Gram-negative bacteria were predominant.

Discrepancies in the recovery of bacteria from multiple sinuses

Differences exist in the distribution of bacteria in a single patient with infections in multiple sinuses. Brook evaluated the differences in the microbiology in 155 patients with multiple chronically infected sinuses [78]. The patients had sinusitis of either the maxillary, ethmoid, or frontal sinuses (any combination) and had organisms isolated from two to four concomitantly infected sinuses. In patients who had organisms isolated from two sinuses and had acute sinusitis, 31 (56 %) of the 55 isolates were found only in a single sinus, and 24 (44 %) were recovered concomitantly from two sinuses. In those with chronic infection, 31 (34 %) of the 91 isolates were recovered only from a single sinus, and 60 (66 %) were found concomitantly from two sinuses. Anaerobic bacteria were more often concomitantly isolated from two sinuses (50 of 70) than aerobic and facultative bacteria (10 of 21, $p < 0.05$). Similar findings were present in those who had organisms recovered from three or four sinuses. BLPB were more often isolated from patients with chronic infection (58–83 %) as compared to those with acute infections (32–43 %). These observations show that there are differences in the distribution of organisms in a single patient who suffers from infections in multiple sinuses and emphasizes the importance of obtaining cultures from all infected sinuses.

Beta lactamase producing bacteria

Staphylococcus aureus, *H. influenzae*, *M. catarrhalis*, and pigmented *Prevotella*, and *Fusobacterium* species can produce the enzyme beta-lactamase [78]. The recovery rate of aerobic and anaerobic BLPB in the oropharynx has increased in recent years, and these organisms were isolated in over half of the patients with head and neck infections, including sinusitis [79]. BLPB can be involved directly in the infection, protecting not only themselves from the activity of penicillins, but also penicillin-susceptible organisms. This can occur

when the enzyme beta-lactamase is secreted into the infected tissue or abscess fluid in sufficient quantities to break the penicillins' beta-lactam ring before it can kill the susceptible bacteria [80].

The high incidence of the recovery of BLPB in upper respiratory tract infections may be due to the selection of these organisms following antimicrobial therapy with beta-lactam antibiotics. The emergence of penicillin-resistant flora can occur following only a short course of penicillin [81, 82].

The actual activity of the enzyme beta-lactamase and the phenomenon of “shielding” were demonstrated in acutely and chronically inflamed sinuses fluids [83]. BLPB were isolated in 4 of 10 acute sinusitis (Table 3) aspirates and in 10 of 13 CRS aspirates. The predominate BLPB isolated in acute sinusitis were *H. influenzae* and *M. catarrhalis*, and those found in CRS were *Prevotella* and *Fusobacterium* spp. The recovery of BLPB is not surprising, since over two-thirds of the patients with acute and all of the patients with CRS received antimicrobial agents that might have selected for BLPB.

Summary

There are significant differences in the microbiology of CRS as compared with acute sinusitis. *Staphylococcus aureus*, *S. epidermidis*, and anaerobic Gram-negative bacteria predominate in CRS. The persistence of the infection can promote the growth of anaerobic bacteria. However, the true prevalence of anaerobic bacteria in CRS is misrepresented in studies that did not use methods adequate for their recovery.

Familiarization with the microbiology of CRS is of great importance when selecting empirical antimicrobial therapy. Selection of the appropriate antimicrobial agent(s) is generally

Table 3 Beta-lactamase-producing organisms detected in CRS aspirates [83]

Organism	Beta-lactamase detected in chronic sinusitis aspirates			
	Patient no.			
	1	2	3	4
<i>Staphylococcus aureus</i> (BL+)		+		+
<i>Streptococcus pneumoniae</i>	+			
<i>Peptostreptococcus</i> spp.	+			+
<i>Propionibacterium acnes</i>	+			
<i>Fusobacterium</i> spp. (BL+)		+		+
<i>Fusobacterium</i> spp. (BL-)		+		+
<i>Prevotella</i> spp. (BL+)			+	
<i>Prevotella</i> spp. (BL-)	+	+	+	
<i>Bacteroides fragilis</i> group (BL+)	+			+
Beta-lactamase activity in pus	+	+	+	+

BL+ = beta-lactamase-producing bacteria

made on an empirical basis. However, in patients who fail to show significant improvement or exhibit deterioration despite therapy, it is important to obtain a culture through sinus puncture or endoscopically.

Compliance with ethical standards

Conflict of interest There is no financial support or conflict of interest for this manuscript.

Ethical approval Not applicable.

Informed consent Not applicable.

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