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Bacteriology of Moderate-to-Severe Diabetic Foot Infections and In Vitro Activity of Antimicrobial Agents▽

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As part of a United States-based multicenter clinical trial, conducted from 2001 to 2004, that compared ertapenem to piperacillin-tazobactam for the treatment of moderate-to-severe diabetic foot infections (DFIs), we obtained 454 pretreatment specimens from 433 patients. After debridement, the investigators collected wound specimens, mostly by curettage or biopsy, and sent them to the R. M. Alden Research Laboratory for aerobic and anaerobic culture. Among the 427 positive cultures, 83.8% were polymicrobial, 48% grew only aerobes, 43.7% had both aerobes and anaerobes, and 1.3% had only anaerobes. Cultures yielded a total of 1,145 aerobic strains and 462 anaerobic strains, with an average of 2.7 organisms per culture (range, 1 to 8) for aerobes and 2.3 organisms per culture (range, 1 to 9) for anaerobes. The predominant aerobic organisms were oxacillin-susceptible *Staphylococcus aureus* (14.3%), oxacillin-resistant *Staphylococcus aureus* (4.4%), coagulase-negative *Staphylococcus* species (15.3%), *Streptococcus* species (15.5%), *Enterococcus* species (13.5%), *Corynebacterium* species (10.1%), members of the family *Enterobacteriaceae* (12.8%), and *Pseudomonas aeruginosa* (3.5%). The predominant anaerobes were gram-positive cocci (45.2%), *Prevotella* species (13.6%), *Porphyromonas* species (11.3%), and the *Bacteroides fragilis* group (10.2%). Pure cultures were noted for 20% of oxacillin-resistant *Staphylococcus aureus* cultures, 9.2% of *Staphylococcus epidermidis* cultures, and 2.5% of *P. aeruginosa* cultures. Two or more species of *Staphylococcus* were present in 13.1% of the patients. Ertapenem and piperacillin-tazobactam were each active against >98% of the enteric gram-negative rods, methicillin-sensitive *S. aureus*, and anaerobes. Among the fluoroquinolones, 24% of anaerobes, especially the gram-positive cocci, were resistant to moxifloxacin; 27% of the gram-positive aerobes but only 6% of the members of the family *Enterobacteriaceae* were resistant to levofloxacin. Moderate-to-severe DFIs are typically polymicrobial, and almost half include anaerobes. Our antibiotic susceptibility results can help to inform therapeutic choices.

While foot infections in persons with diabetes are initially treated empirically, therapy directed at known causative organisms may improve the outcome. Many studies have reported on the bacteriology of diabetic foot infections (DFIs) over the past 25 years, but the results have varied and have often been contradictory. A number of studies have found that *Staphylococcus aureus* is the main causative pathogen (12, 34, 35), but two recent investigations reported a predominance of gram-negative aerobes (20, 47). The role of anaerobes is particularly unclear, because in many studies specimens were not collected or cultured properly to recover these organisms. Among those that did use appropriate methods, some report that anaerobes play a minimal role (2, 7, 15, 21, 46), while others suggest that *Bacteroides fragilis* is the predominant anaerobe isolated (1, 3, 17, 57).

These discrepancies could be partly due to differences in the causative organisms occurring over time, geographical variations, or the types and severity of infection included in the studies (1, 20, 47, 51). In addition, some studies used a relatively small number of specimens, failed to report recent or concomitant antibiotic therapy, did not ensure that the specimen collection techniques would exclude superficial or colonizing organisms, or even make clear whether or not the wound was clinically infected. Also, laboratory processing of the samples may have been inadequate to grow anaerobes or fastidious organisms, and protocols that classify potential pathogens (e.g., coagulase-negative staphylococci [CoNS] or *Corynebacterium* species) as colonizers may have been used (4, 46, 49).

While *S. aureus* and beta-hemolytic streptococci are widely recognized as pathogens in early DFIs, the role of other frequently isolated organisms is less clear to both the clinician and the microbiology laboratory. Previous studies have shown that when optimal specimen collection, transport, and culture techniques are used, multiple organisms are usually recovered from DFIs (6, 14, 23, 29, 30, 45, 55). Furthermore, some studies suggest that the interactions of organisms within these polymicrobial mixtures lead to the production of virulence factors, such as hemolysins, proteases, and collagenases, as well as short-chain fatty acids, that cause inflammation, impede wound healing, and contribute to the chronicity of the infection (5, 52, 53, 56). In such mixtures, biofilms that impede the penetration of antimicrobial agents into the infected site may also form (25). Thus, the presence of multiple species can have important clinical implications that should not be overlooked (5, 23).

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To better define the bacteriology of DFIs, we analyzed our data from a large prospective multicenter trial, recently performed in the United States, that investigated the outcome of treatment for diabetic patients who had moderate-to-severe lower-extremity infections that required (at least initial) parenteral antibiotic therapy. This study used well-defined collection procedures, excluded patients who had recently received systemic antibiotic therapy, and had the specimens sent to the R. M. Alden Research Laboratory, where optimal microbiological culture techniques were used.

MATERIALS AND METHODS

The specimens used in this study were obtained from a clinical trial (the SIDESTEP trial) that was designed to compare ertapenem and piperacillin-tazobactam for the treatment of DFIs that required parenteral therapy, at least initially (33). The trial enrolled diabetic male and female adults who had clinically infected wounds that were moderate or severe by definitions compatible with the Infectious Diseases Society of America guidelines (34) and who had not received systemic antibiotic therapy for more than 24 h within the previous 72 h, if they met other selected criteria. The protocol called for the exclusion of patients with osteomyelitis or limb ischemia requiring revascularization.

To avoid the isolation of colonizing (rather than pathogenic) flora, the investigators were instructed to first clean and debride all foot wounds and to obtain specimens by tissue biopsy, wound curettage, or aspiration rather than swab techniques. Investigators then placed the specimens into sterile anaerobic transport tubes (Anaerobe Systems, Morgan Hill, CA) and shipped them to the R. M. Alden Research Laboratory by overnight courier. Upon receipt, we took the specimens into an anaerobic chamber, inoculated them onto anaerobic media (brucella agar supplemented with vitamin K_1, hemin, and 5% sheep blood; brucella agar with laked blood, kanamycin, and vancomycin; phenylethyl alcohol brucella blood agar; and bacteroides-bile-esculin agar [Anaerobe Systems]), and incubated the plates at 37°C for 4 to 5 days. Aerobic cultures were plated onto Trypticase soy blood agar and Rose agar and incubated at 35°C in 5% CO_2 and onto MacConkey agar (Hardy Diagnostics, Santa Maria, CA) and incubated at 35°C in ambient air. Isolates were identified by standard methods (31, 38). In some instances, we identified unusual strains using partial 16S rRNA gene sequencing (54).

We performed susceptibility testing in accordance with Clinical and Laboratory Standards Institute (formerly NCCLS) procedures: aerobic organisms were tested by the broth microdilution method with cation-adjusted Mueller-Hinton broth (9); tests for streptococci and aerobic gram-positive rods were supplemented with 2.5% laked horse blood, and the aerobic gram-positive rods were incubated for 48 h (10). For anaerobic bacteria, we used the agar dilution method with supplemented brucella agar and a final inoculum of 10^5 CFU/spot (11).

RESULTS

We cultured a total of 454 specimens and isolated 1,607 organisms, as shown in Table 1. Of the 427 culture-positive specimens, 16.2% had growth of a single organism, while the rest were polymicrobial, with 43.7% yielding four or more organisms. A total of 1,145 aerobic organisms were recovered, with a range of 0 to 8 species per specimen and an average of 2.7 species per positive specimen. The total number of anaerobes was 462, with a range of 0 to 9 species per specimen and an average of 2.3 species per positive specimen. The range of all organisms was 1 to 13 per positive specimen, with an average of 3.8 species per positive specimen.

The methods used to collect the specimens and the types of isolates obtained from these specimen types are shown in Table 2. Tissue biopsy of specimens was the most frequent method (57%), while needle aspiration was the least frequent method but yielded the greatest proportion of pure cultures. Despite instructions to the investigators to avoid the use of swabs for culture, swabs constituted over a quarter of the specimens. The distribution of the major groups of organisms shows that anaerobic organisms and *Staphylococcus epidermidis* were isolated the most frequently from tissue specimens.

TABLE 1. Characteristics of diabetic foot specimens taken prior to antimicrobial therapy

Characteristic	Value
Total no. of specimens	454
No. (%) with aerobes only	222 (48.9)
No. (%) with anaerobes only	6 (1.3)
No. (%) with mixed growth	199 (43.8)
No. (%) with no growth	27 (5.9)
No. of positive cultures	427
No. of patients with positive cultures	406
No. (%) of positive cultures with:	
One isolate	69 (16.2)
Two isolates	87 (20.4)
Three isolates	84 (19.7)
Four isolates	57 (13.3)
More than four isolates	130 (30.4)
Total no. of aerobes	1,145
No. of different species	115
Range of no. of aerobes per specimen	0–8
Avg no. of aerobes per positive specimen	2.7
No. (%) of positive specimens in pure culture	64 (15.2)
Total no. of anaerobes	462
No. of different species	74
Range of no. of anaerobes per specimen	0–9
Avg no. of anaerobes per positive specimen	2.3
No. (%) of positive specimens in pure culture	3 (1.5)
Total no. of all isolates	1,607

Table 3 presents the distribution of organisms found in the DFIs. Gram-positive species comprised 80.3% (920 of 1,145) of the aerobic organisms and 57.2% (920 of 1,607) of all strains. The predominant aerobic species was *S. aureus*, 76.6% (164 of 214) of the isolates of which were oxacillin susceptible. CoNS, with 175 isolates, were the second most frequently encountered organisms. Of note is that most of these were cultured from tissue specimens. *S. epidermidis* accounted for 49.7% of the CoNS isolates, with 9.2% (8 of 87) isolated in pure culture. *Staphylococcus lugdunensis* was cultured from 22 specimens, including as a single isolate from two patients, and *Staphylococcus haemolyticus* was recovered from 22 specimens, 1 of which was in pure culture. Other species of staphylococci included 12 strains of *Staphylococcus simulans*, 2 of which were recovered in pure culture, and 4 strains of *Staphylococcus hominis.* Streptococci were the next most frequently cultured group and comprised 15.5% (177 of 1,145) of all aerobic strains, with *Streptococcus agalactiae* accounting for almost half of these (48.6%) and the *Streptococcus mitis* and *Streptococcus milleri* groups accounting for 33.8% (60 of 177). Only three isolates of *Streptococcus pyogenes* were recovered. Enterococci were found in 35.7% of the patients; and other cocci such as *Helcococcus*, *Aerococcus*, and *Gemella* were present in smaller numbers. A variety of aerobic gram-positive rods were detected, including *Corynebacterium amycolatum* (49 isolates), followed by *Corynebacterium striatum* ($n = 30$), *Corynebacterium jeikeium*, *Corynebacterium tuberculostearicum*, and *Corynebacterium xerosis*.

TABLE 2. Comparative frequency of groups of species by specimen collection type

Organism	No. of isolates (% of specimens yielding the group[a]) obtained by or with:				
	Total (n = 454)	Aspiration (n = 52 [11.5[b]])	Swab (n = 132 [29.1])	Tissue (n = 258 [56.8])	Not specified (n = 12 [2.6])
Aerobes					
Nonfermenting gram-negative rods	35 (7.7)	5 (9.6)	10 (7.6)	18 (7.0)	2 (16.7)
Pseudomonas spp.	42 (9.3)	3 (5.8)	15 (11.4)	24 (9.3)	0
Enterobacteriaceae group	147 (32.4)	16 (30.8)	45 (34.1)	85 (32.9)	1 (8.3)
Corynebacterium spp.	116 (25.6)	7 (13.5)	32 (24.2)	72 (27.9)	5 (41.7)
Miscellaneous gram-positive rods	53 (11.7)	3 (5.8)	18 (13.6)	32 (12.4)	0
Enterococcus spp.	154 (33.9)	10 (19.2)	56 (42.4)	84 (32.6)	4 (33.3)
Staphylococcus spp.	388 (85.5)	34 (65.4)	107 (81.1)	237 (91.9)	10 (83.3)
S. aureus, Ox-R[c]	53 (11.7)	4 (7.7)	20 (15.2)	24 (9.3)	1 (8.3)
S. aureus, Ox-S[d]	164 (36.1)	22 (42.3)	46 (34.8)	93 (36.0)	3 (25.0)
S. epidermidis	72 (15.9)	2 (3.8)	21 (15.9)	47 (18.2)	2 (16.7)
S. epidermidis, Ox-R	15 (3.3)	0	6 (4.5)	9 (3.5)	
S. haemolyticus	22 (4.8)	1 (1.9)	4 (3.0)	16 (6.2)	1 (8.3)
S. lugdunensis	22 (4.8)	1 (1.9)	4 (3.0)	14 (5.4)	3 (25.0)
Other coagulase-negative staphylococci	36 (7.9)	3 (5.8)	7 (5.3)	26 (10.1)	
Streptococcus spp.	190 (41.9)	23 (44.2)	48 (36.4)	110 (42.6)	9 (75.0)
Anaerobes					
Bacteroides fragilis group	55 (12.1)	4 (7.7)	16 (12.1)	32 (12.4)	3 (25.0)
Fusobacterium spp.	11 (2.4)	1 (1.9)	3 (2.3)	7 (2.7)	
Porphyromonas spp.	53 (11.7)	4 (7.7)	12 (9.1)	37 (14.3)	
Prevotella spp.	64 (14.1)	2 (3.8)	15 (11.4)	46 (17.8)	1 (8.3)
Anaerobic cocci	219 (48.2)	14 (26.9)	65 (49.2)	133 (51.6)	7 (58.3)
Clostridium spp.	20 (4.4)	3 (5.8)	7 (5.3)	10 (3.9)	
Non-spore-forming, gram-positive rods	43 (9.5)	2 (3.8)	11 (8.3)	29 (11.2)	1 (8.3)

[a] Percent represents the percentage of each type of specimen yielding the indicated organism group.
[b] Values in brackets are the percentage of all specimens.
[c] Ox-S, oxacillin sensitive.
[d] Ox-R, oxacillin resistant.

One isolate each of *Corynebacterium urealyticum* and *Corynebacterium amycolatum* were recovered in pure culture.

Gram-negative rods comprised 19.7% (225 of 1,145) of the aerobic organisms. *Pseudomonas aeruginosa* was the predominant species, but only 1 of 40 patients had this organism in a pure culture. *Proteus mirabilis* and *Klebsiella* species were the next most often recovered gram-negative aerobes. Members of the family *Enterobacteriaceae* were the largest group of aerobic gram-negative rods and comprised 63.3% (147 of 225) of all gram-negative species.

Anaerobes were found in 49% of patients, with gram-positive cocci accounting for 45.5% of all anaerobes. *Finegoldia magna* was the predominant anaerobic species and was found in 24.4% (99 of 406) of the patients. *Prevotella* species were the second most common (12.3% of patients), followed by *Porphyromonas* species (10.3%) and the *Bacteroides fragilis* group (10.2%). *B. fragilis* was the predominant species (40.4%; 19 of 47) within the *B. fragilis* group.

The antimicrobial susceptibilities of the organisms that were isolated are shown in Tables 4 to 6. All aerobic gram-positive strains (Table 4) were fully susceptible to vancomycin, daptomycin, and linezolid (data not shown). Piperacillin-tazobactam and amoxicillin-clavulanate were the next most active drugs against the gram-positive aerobes, with resistance noted only in oxacillin-resistant *Staphylococcus aureus* (methicillin-resistant *S. aureus* [MRSA]), certain strains of CoNS, and several species of corynebacteria. Ertapenem was also active against the majority of strains, excluding the enterococci and MRSA strains. Cephalexin, clindamycin, and ciprofloxacin were noticeably less active than the other agents tested. Ciprofloxacin was the least active of the quinolones, especially against all species of streptococci; moxifloxacin was the most active quinolone, with an MIC of ≤ 1 μg/ml for 79% of the strains. Many strains of streptococci, most notably, *S. agalactiae*, and many enterococci were resistant to doxycycline, while 16% of the *Streptococcus* species were resistant to clindamycin.

Among the gram-negative organisms (Table 5), *Stenotrophomonas maltophilia* was resistant to most agents tested. *P. aeruginosa* strains and the *Enterobacteriaceae* group were largely susceptible to imipenem, piperacillin-tazobactam, ceftazidime, aminoglycosides, and ciprofloxacin. Piperacillin-tazobactam and the quinolones were active against more than 90% of the gram-negative organisms, while amoxicillin-clavulanate, doxycycline, and cephalexin were the least active of the drugs tested. Ertapenem is known to have poor activity against *P. aeruginosa*.

Among the anaerobes (Table 6), all isolates were susceptible to ertapenem; and all but two strains, one *B. fragilis* strain and one *Bacteroides vulgatus* strain, were susceptible to piperacillin-tazobactam. Amoxicillin-clavulanate was active against all except 10 strains of the *B. fragilis* group. Overall, 18% of the anaerobes were resistant to clindamycin and 24% were resis-

TABLE 3. Distribution of 462 anaerobes and 1,145 aerobes isolated from DFIs

Organism	No. isolated	% Total aerobes or anaerobes	% in genus	% Total isolates	No. (%) of patients[a]	No. (%) in pure culture
All gram-positive aerobes	920	80.3		57.1	394 (97.0)	63 (6.8)
Staphylococcus spp.	389	34.0		24.1	328 (80.8)	
OSSA[b]	164	14.3	42.2	10.2	162 (39.9)	26 (15.9)
ORSA[c]	50	4.4	12.9	3.1	48 (11.8)	10 (20)
S. epidermidis (15 MRSE[d] strains)	87	7.6	22.4	5.4	81 (20.0)	8 (9.2)
S. lugdunensis	22	1.9	5.7	1.4	22 (5.4)	2 (9.1)
S. haemolyticus	22	1.9	5.7	1.4	20 (4.9)	1 (4.5)
S. simulans	12	1.0	3.1	0.7	12 (3.0)	2 (16.7)
Other *Staphylococcus* spp.	32	2.8	8.2	2.0	31 (7.6)	2 (9.4)
Streptococcus spp.	177	15.5		10.5	168 (41.1)	
S. agalactiae	86	7.5	48.6	5.2	82 (20.2)	3 (3.5)
S. mitis group	41	3.6	23.2	2.5	38 (9.4)	2 (4.9)
S. milleri group	19	1.7	10.7	1.1	17 (4.2)	
S. dysgalactiae subsp. *equisimilis*	18	1.6	10.2	1.1	18 (4.4)	
Other *Streptococcus* spp., including *S. pyogenes* ($n = 3$)	13	1.1	7.3	1.1	13 (3.2)	
Miscellaneous gram-positive cocci	27	2.4		1.7		1 (3.7)
Enterococcus spp.	155	13.5		9.6	145 (35.7)	
E. faecalis	138	12.1	89.0	8.6	128 (31.5)	1 (0.7)
Other *Enterococcus* spp.	17	1.5	11.0	1.1	17 (4.2)	1 (5.9)
Corynebacterium spp.	116	10.1		7.2	115 (28.3)	
C. amycolatum	49	4.3	42.2	3	46 (11.3)	1 (2.0)
C. striatum	30	2.6	25.9	1.9	29 (7.1)	
Other *Corynebacterium* spp.	37	3.2	31.9	2.3	37 (9.1)	1 (2.7)
Dermabacter hominis	15	1.3	11.5	0.9	15 (3.4)	
Actinomyces-Arcanobacterium group	13	1.1				
Other gram-positive rods	25	2.2				1 (4.0)
All gram-negative aerobic organisms	225	19.7		14.0	145 (35.7)	3 (1.3)
Escherichia coli	20	1.7	8.9	1.2	20 (4.9)	
Klebsiella spp.	25	2.2	11.1	1.6	25 (6.2)	
Enterobacter cloacae	20	1.7	8.9	1.2	20 (4.9)	1 (5.0)
Enterobacter-Citrobacter-Pantoeae group	16	1.4	7.1	1.0	13 (3.2)	1 (6.3)
Serratia marcescens	14	1.2	6.2	0.9	14 (3.4)	
Proteus-Providencia-Morganella group	28	2.4	12.4	1.7	25 (6.2)	
Proteus mirabilis	24	2.1	10.7	1.5	23 (5.7)	
Pseudomonas aeruginosa	40	3.5	17.8	2.5	35 (8.6)	1 (2.5)
Stenotrophomonas maltophilia	15	1.3	6.7	0.9	15 (3.7)	
Alcaligenes faecalis group	10	0.9	4.4	0.6	9 (2.2)	
Other nonfermenting gram-negative rods	13	1.1	5.8	0.8	13 (3.2)	
All anaerobic organisms	462			28.7[e]	199 (49.0)	3 (0.6)
Bacteroides fragilis group	47	10.2		2.9	34 (8.4)	
B. fragilis	19	4.1	40.4			
B. caccae	2	0.4	4.3			
B. distasonis	1	0.2	2.1			
B. ovatus	5	1.1	10.6			
B. stercoris	2	0.4	4.3			
B. thetaiotaomicron	8	1.7	17.0			
B. uniformis	5	1.1	10.6			
B. vulgatus	5	1.1	10.6			
Prevotella spp.	63	13.6		3.9	50 (12.3)	
P. melaninogenica	11	2.4	17.2		10 (2.5)	
Prevotella spp., pigmented	10	2.2	15.6			
Prevotella bivia	26	5.8	41.3		26 (6.4)	
Prevotella spp., nonpigmented	16	3.5	25.0			

Continued on following page

TABLE 3—*Continued*

Organism	No. isolated	% Total aerobes or anaerobes	% in genus	% Total isolates	No. (%) of patients[a]	No. (%) in pure culture
Porphyromonas spp.	52	11.3		3.3	42 (10.3)	
P. asaccharolytica	29	6.3	55.8		28 (6.9)	
P. somerae (formerly *P. levii*)	21	4.5	39.6		20 (4.9)	
Other *Porphyromonas* spp.	2	0.4	3.8			
Fusobacterium spp.	11	2.4		0.7	10 (2.5)	
F. nucleatum	8	1.7	72.7			
F. mortiferum-F. varium group	3	0.6	27.2			
Other gram-negative species	13	2.8		0.8		
Anaerobic gram-positive cocci	209	45.2		13.0	152 (37.4)	
Finegoldia magna	102	22.1	48.8	6.4	99 (24.4)	
Peptoniphilus asaccharolyticus	37	8.0	17.7		37 (9.1)	
Peptostreptococcus anaerobius	15	3.2	7.2		14 (3.4)	
Anaerococcus prevotii	13	2.8	6.2		13 (3.2)	1 (7.7)
Anaerococcus tetradius	9	1.9	4.3		9 (2.2)	
Peptostreptococcus micros	6	1.3	2.9		6 (1.5)	
Other species	27	5.8	12.9		27 (6.7)	
Clostridium spp.	20	4.3		1.2	20 (4.9)	
C. innocuum	1	0.2	5.0			
C. clostridioforme group	3	0.6	15.0			
C. perfringens	6	1.3	30.0			
Other *Clostridium* spp.	10	2.1	50.0			
Eubacterium group	17	3.7		1.1	17 (4.2)	
Other gram-positive, non-spore-forming rods[f]	30	6.5		1.9		2 (6.7)

[a] A total of 406 patients had positive cultures.
[b] OSSA, oxacillin-sensitive *S. aureus*.
[c] ORSA, oxacillin-resistant *S. aureus*.
[d] MRSE, methicillin-resistant *S. epidermidis.*
[e] Of a total of 1,607 isolates.
[f] Including *Lactobacillus* spp., *Propionibacterium* spp., and *Actinomyces* spp.

tant to moxifloxacin (MICs $\geq$ 4 μg/ml). Although the breakpoints for levofloxacin against anaerobes have not been defined, 45% of the strains required levofloxacin concentrations $\geq$4 μg/ml to inhibit their growth.

DISCUSSION

DFIs are a major and increasing problem worldwide. In the United States about 25% of the more than 18 million diabetic patients develop foot ulcerations during their lifetimes, and over half of these become infected (32). To avoid selective antibiotic pressure that fosters the development of resistance, most authorities advocate treatment only for clinically infected wounds and use of the narrowest-spectrum therapy possible (33). On the other hand, failure to treat appropriately patients with these potentially limb-threatening infections can result in a poor outcome. Our study shows that in patients with moderate to severe DFIs who have not recently received antibiotic therapy, these infections are generally polymicrobial, with mixed gram-positive and gram-negative species and an average of 2.7 aerobic bacteria and a average of 2.3 anaerobic bacteria per culture-positive specimen.

Staphylococcal species comprised 24.1% of all isolates recovered; 55% of these were *S. aureus*, with 16.8% isolated in pure culture. These results are compatible with the findings of other studies (25, 34, 54). Most of the methicillin-sensitive strains were susceptible to all the antibiotics that we tested. CoNS comprised 45% of the staphylococcal species recovered, and more than one species was present in 46 specimens. Some strains of CoNS displayed a high degree of resistance to many of the antibiotics, as previously reported by others (20, 26, 50).

Staphylococcus epidermidis comprised nearly 50% of the CoNS; 9.2% of these isolates were in pure culture and 17.2% were methicillin resistant. Often dismissed as a contaminant or colonizer, *S. epidermidis* is increasingly being recognized as a true pathogen. This is especially true not only in nosocomial infections involving catheters and prosthetic devices but also in various other types of wound infections (43, 56). Although it is innocuous on intact human skin, it can cause severe infections after it penetrates anatomic barriers (56), partly by producing proteases, peptidases, biofilms, and surface lipoproteins that promote host tissue adherence. Several genes, such as *icaABC* and IS*256*, are being investigated by others as possible discriminators for virulent versus commensal strains (25, 52, 56), and von Eiff et al. noted that the production of bacteriocins by *S. epidermidis* may play a substantial role in excluding competing organisms (52). Interestingly, while we found *S. epidermidis* coexisting with a variety of other organisms, it was never found in specimens that had MRSA. We found that CoNS were also

TABLE 4. In vitro activities of antimicrobial agents against gram-positive aerobic organisms

Organism (no. of isolates)	MIC_{50}/MIC_{90} (μg/ml [% susceptible])[a]									
	ETP	P/T	A/C	CFL	CIP	LVX	MXF	DOX	CM	T/S
Corynebacterium amycolatum (49)	2/>16 (69)	≤2/>32 (78)	≤1/>8 (78)	≤2/>32 (55)	8/>8 (27)	8/>8 (27)	2/>4 (57)	≤2/16 (80)	8/>8 (10)	2/>4 (51)
Corynebacterium spp. and other non-spore-forming gram-positive rods[b] (120)	≤0.25/2 (93)	≤2/>32 (78)	≤1/4 (91)	≤2/>32 (74)	4/>8 (50)	2/>8 (54)	0.5/>4 (74)	≤2/8 (87)	8/>8 (30)	4/>4 (49)
Enterococcus spp.[c] (155)	8/16 (10)	≤2/>32 (97)	≤1/≤1 (99)	>32/>32 (5)	1/>8 (68)	1/>8 (77)	0.5/>4 (80)	4/8 (63)	>8/>8 (1)	≤0.5/4 (90)
Staphylococcus aureus, Ox-R[d] (49)	4/>16 (NI[e])	8/32 (NI)	8/>8 (NI)	>32/>32 (NI)	>8/>8 (12)	>8/>8 (16)	4/>4 (16)	≤2/≤2 (94)	>8/>8 (47)	≤0.5/≤0.5 (90)
S. aureus, Ox-S[f] (169)	≤0.25/≤0.25 (100)	≤2/≤2 (100)	≤1/≤1 (100)	≤2/4 (99)	≤0.5/1 (94)	≤0.5/≤0.5 (96)	≤0.25/≤0.25 (95)	≤2/≤2 (95)	≤0.25/≤0.25 (98)	≤0.5/≤0.5 (98)
S. epidermidis (89)	2/8 (87)	≤2/≤2 (97)	≤1/2 (99)	16/32 (37)	≤0.5/>8 (54)	≤0.5/8 (57)	≤0.25/2 (63)	≤2/8 (90)	≤0.25/>8 (89)	≤0.5/>4 (67)
S. haemolyticus (22)	2/>16 (68)	≤2/>32 (68)	≤1/>8 (68)	>32/>32 (14)	>8/>8 (18)	8/>8 (23)	1/>4 (23)	≤2/32 (55)	≤0.25/>8 (77)	≤0.5/>4 (68)
S. lugdunensis (23)	≤0.25/≤0.25 (100)	≤2/≤2 (100)	≤1/≤1 (100)	4/16 (83)	≤0.5/≤0.5 (100)	≤0.5/≤0.5 (100)	≤0.25/≤0.25 (100)	≤2/≤2 (100)	≤0.25/≤0.25 (91)	≤0.5/≤0.5 (100)
Coagulase-negative *Staphylococcus* spp.[g] (44)	0.5/4 (93)	≤2/≤2 (98)	≤1/2 (100)	≤2/>32 (77)	≤0.5/>8 (80)	≤0.5/>8 (82)	≤0.25/4 (82)	≤2/4 (96)	≤0.25/>8 (84)	≤0.5/1 (91)
Streptgoccus spp.[h] (173)	≤0.25/≤0.25 (100)	≤2/≤ (100)	≤1/≤1 (99)	≤2/8 (93)	≤0.5/4 (71)	≤0.5/2 (97)	≤0.25/0.5 (97)	8/16 (40)	≤.25/>8 (90)	≤0.5/≤0.5 (95)

[a] ETP, ertapenem; P/T, piperacillin-tazobactam; A/C, amoxicillin-clavulanic acid; CFL, cephalexin; CIP, ciprofloxacin; LVX, levofloxacin; MXF, moxifloxacin; DOX, doxycycline; CM, clindamycin; T/S, trimethoprim-sulfamethoxazole.

[b] *Corynebacterium striatum* ($n = 31$), *Corynebacterium accolens* ($n = 1$), *Corynebacterium aurimucosum* ($n = 5$), *Corynebacterium glucuronolyticum* ($n = 2$), *Corynebacterium jeikeium* ($n = 5$), *Corynebacterium minutissimum* ($n = 1$), *Corynebacterium pseudodiphtheriticum* ($n = 1$), "*Corynebacterium pseudogenitalium*" ($n = 2$), *Corynebacterium pseudotuberculosis* ($n = 1$), *Corynebacterium simulans* ($n = 4$), *Corynebacterium tuberculostearicum* ($n = 7$), *Corynebacterium urealyticum* ($n = 1$), *Corynebacterium xerosis* ($n = 4$), *Corynebacterium* spp. ($n = 2$), *Dermabacter hominis* ($n = 15$), *Actinobaculum massiliae* ($n = 1$), *Actinomyces neuii* subsp. *anitratus* ($n = 2$), *A. neuii* subsp. *neuii* ($n = 1$), *A. turicensis* ($n = 2$), *Arcanobacterium bernardiae* ($n = 5$), *Arcanobacterium hemolyticum* ($n = 3$), *Arthrobacter albus* ($n = 2$), *Arthrobacter creatinolyticus* ($n = 1$), *Bacillus cereus* ($n = 2$), *Bacillus pumilus* ($n = 2$), *Bacillus* sp. ($n = 1$), *Bifidobacterium urinalis* ($n = 1$), *Brachybacterium* sp. ($n = 1$), *Brevibacterium lutoleum* ($n = 1$), *Brevibacterium otitidis* ($n = 1$), *Brevibacterium* spp. ($n = 2$), *Lactobacillus gasseri* ($n = 1$), *Lactobacillus jensenii* ($n = 1$), *Microbacterium oxydans* (2), *Paenibacillus* sp. ($n = 1$), *Propionibacterium acnes* ($n = 1$) and *Propionibacterium avidum* ($n = 1$) (both aerobic), "*Zimmermannella bifida*" ($n = 1$), and gram-positive bacilli with no sequence match ($n = 2$).

[c] *Enterococcus faecalis* ($n = 139$), *E. avium* ($n = 3$), *E. canis* ($n = 2$), *E. casseliflavus* ($n = 1$), *E. faecium* ($n = 5$), *E. gallinarum* ($n = 4$), and *Enterococcus* sp. ($n = 1$).

[d] Ox-S, oxacillin sensitive.

[e] NI, no interpretation.

[f] Ox-R, oxacillin resistant.

[g] *Staphylococcus. auricularis* ($n = 1$), *S. capitis* ($n = 2$), *S. caprae* ($n = 3$), *S. cohnii* ($n = 4$), *S. hominis* ($n = 5$), *S. schleiferi* ($n = 1$), *S. sciuri* ($n = 9$), *S. simulans* ($n = 12$), *S. warneri* ($n = 4$), *S. xylosus* ($n = 1$), and *Staphylococcus* spp. with no sequence match ($n = 2$).

[h] *Streptococcus agalactiae* ($n = 85$), *S. anginosus* ($n = 17$), *S. bovis* ($n = 1$), *S. canis* ($n = 1$), *S. constellatus* ($n = 2$), *S. dysgalactiae* subsp. *equisimilis* ($n = 19$). *S. gordonii* ($n = 1$), *S. infantarius* ($n = 1$), *S. mitis* group ($n = 41$), *S. minor* ($n = 1$), *S. pyogenes* ($n = 3$), and *S. salivarius* ($n = 1$).

most often isolated from tissue specimens, which are less likely to harbor contaminants or colonizers.

Other CoNS that we isolated, including *S. haemolyticus*, *S. hominis*, and *S. simulans*, are also being increasingly recognized as pathogens in various types of infections (19, 42, 44). *Staphylococcus lugdunensis*, another organism isolated in our study, is not usually identified in DFIs, although Herchline and Ayers reported it to be a prominent and sometimes sole pathogen in skin and skin structure infections (28). Although *S. lugdunensis* is normally associated with osteomyelitis or other bone infections (24), we found it in pure culture for 2 of 22 patients, as well as in the single bone specimen available in our study. This organism resembles *S. aureus* more than other coagulase-negative species in its ability to cause serious infections that are mediated in part by the production of virulence factors, such as clumping factor, a thermostable DNase, esterase, lipase, protease, and a fatty acid-modifying enzyme (27, 52).

Streptococci were cultured from 41% of the patients, with *S. agalactiae* comprising almost half of the strains. This is a well-recognized pathogen in DFIs; but other streptococci, such as those of the *S. milleri* group, which have long been associated with acute and chronic suppurative infections (39), were also present in 4.2% of the patients. These are usually reported as "viridans *Streptococcus* sp." in DFIs and other mixed infections or are considered unimportant and are not reported in such cultures. *Streptococcus dysgalactiae* subsp. *equisimilis* was also present in 4.4% of the patients and has virulence factors similar to those of *S. pyogenes* (13).

Enterococci are considered commensals with low virulence except in compromised patients, such as diabetics, in whom they can act as opportunistic pathogens. We recovered *Enterococcus* species from 35.7% of our patients, including in pure culture from two patients.

Another relatively nonvirulent genus that has been the subject of debate over whether it is a pathogen in DFIs is *Corynebacterium*. We found corynebacteria in 28.3% of the patients. Bessman et al. first raised the issue of the importance of this organism in DFIs (4). In a retrospective review of patients hospitalized for DFIs, they found that corynebacteria were isolated significantly more often from intraoperative specimens (14 of 19 [74%]) than from specimens obtained at the bedside (25 of 65 [39%]). Bowler and Davies also noted the presence of *Corynebacterium* species in infected leg ulcers but not in uninfected leg ulcers (5).

Several studies have investigated the relationship of the specimen collection method to the numbers and the types of organisms recovered from wound infections. Some have found that tissue specimens are more sensitive and specific, containing fewer apparent contaminants and more pathogens than swab cultures (2, 7, 14, 18, 34, 36, 46). Others have reported that with adequate preliminary debridement, the use of a wound swab is as reliable as the use of a tissue specimen, at least for initial monitoring (5, 41, 45, 48). Since our specimens came from many different hospitals across the country, the level of oversight on the collection procedures was limited, although all investigators and study assistants were instructed on the proper methods for the collection of culture materials. Our results show a greater proportion of anaerobes per positive culture from tissue specimens than from swab specimens

TABLE 5. In vitro activities of antimicrobial agents against gram-negative aerobic organisms

Organism (no. of isolates)	MIC_{50}/MIC_{90} (μg/ml [% susceptible])[a]												
	ETP	IPM	P/T	A/C	CFL	CAZ	CIP	LVX	MXF	GM	AMK	DOX	T/S
Enterobacteriaceae group[b] (98)	≤0.125/≤0.125 (99)	0.25/2 (100)	≤1/4 (96)	8/>64 (55)	8/>32 (52)	≤0.5/≤0.5 (94)	≤0.5/≤0.5 (94)	≤0.5/1 (94)	≤0.25/2 (94)	≤2/≤2 (95)	≤8/≤8 (99)	2/16 (79)	≤0.5/>4 (90)
Proteus-Providencia-Morganella group[c] (55)	≤0.125/≤0.125 (98)	4/4 (100)	≤1/≤1 (98)	8/>64 (58)	≤0.5/8 (93)	≤0.5/≤0.5 (95)	≤0.5/≤0.5 (95)	≤0.5/≤0.5 (95)	≤0.25/2 (91)	≤2/≤8 (98)	≤2/≤2 (100)	>32/>32 (22)	≤0.5/>4 (91)
P. aeruginosa (43)	8/16 (NI[d])	1/4 (86)	4/16 (98)		1/4 (98)	≤.5/1 (91)	≤.5/8 (79)	1/8 (74)	≤2/4 (95)	≤8/≤8 (100)			
S. maltophilia (15)	>16 (NI)	>16 (NI)	>128/>128 (NI)	64/64 (NI)	8/>32 (53)	2/>8 (NI)	1/>8 (80)	0.5/4 (NI)	>32/>32 (NI)	128/>128 (NI)	4/4 (ND)	>4/>4 (20)	
Miscellaneous nonfermenting gram-negative rods[e] (24)	≤.125/>16 (63)	0.25/4 (92)	≤1/>128 (79)	4/>64 (67)	4/>32 (79)	1/>8 (58)	≤0.5/>8 (83)	1/>8 (71)	≤2/8 (83)	≤1/128 (79)	≤1/>32 (75)	≤0.5/>4 (75)	

[a] ETP, ertapenem; IPM, imipenem; P/T, piperacillin-tazobactam; A/C, amoxicillin-clavulanic acid; CFL, cephalexin; CAZ, ceftazidime; CIP, ciprofloxacin; LVX, levofloxacin; MXF, moxifloxacin; GM, gentamicin; AMK, amikacin; DOX, doxycycline; T/S, trimethoprim-sulfamethoxazole.

[b] *Escherichia coli* (*n* = 20), *Enterobacter cloacae* (*n* = 21), *Enterobacter aerogenes* (*n* = 7), *Enterobacter gergoviae* (*n* = 1), *Enterobacter intermedius* (*n* = 1), *Citrobacter freundii* (*n* = 1), *Citrobacter koseri* (*n* = 4), *Klebsiella oxytoca* (*n* = 16), *Klebsiella pneumoniae* (*n* = 9), *Pantoeae agglomerans* (*n* = 3), and *Serratia marcescens* (*n* = 15).

[c] *Proteus mirabilis* (*n* = 26), *Proteus vulgaris* (*n* = 4), *Providencia retgeri* (*n* = 6), *Providencia rustigianii* (*n* = 1), *Providencia stuartii* (*n* = 1), and *Morganella morganii* (*n* = 17).

[d] NI, no interpretation.

[e] *Alcaligenes faecalis* (*n* = 10), *Acinetobacter baumannii* (*n* = 6), *Acinetobacter calcoaceticus* (*n* = 1), *Brevundimonas diminuta* (*n* = 1), *Chryseobacterium* sp. (*n* = 1), *Myroides odoratum* (*n* = 1), *Paracoccus* sp. (*n* = 1), *Pseudomonas fluorescens* (*n* = 2), and *Shewanella putrefaciens* (*n* = 1).

TABLE 6. In vitro activities of antimicrobial agents against anaerobic organisms

Organism (no. of isolates)	MIC_{50}/MIC_{90} (μg/ml [% susceptible])[a]					
	ETP	P/T	A/C	CM	LVX	MXF
Bacteroides fragilis group[b] (51)	0.5/4 (100)	2/8 (100)	0.5/8 (80)	1/>32 (67)	8/>16 (33)	2/>16 (57)
Fusobacterium spp.[c] (10)	≤.015/0.25 (100)	≤0.06/2 (100)	≤0.06/0.5 (100)	≤0.06/2 (90)	0.5/4 (80)	0.25/2 (90)
Porphyromonas spp.[d] (53)	≤0.015/≤0.015 (100)	≤0.06/≤0.06 (100)	≤0.06/0.125 (100)	≤0.06/>32 (87)	0.5/2 (91)	0.5/1 (98)
Prevotella spp.[e] (66)	0.125/0.25 (100)	≤0.06/≤0.06 (100)	≤0.25/2 (100)	≤0.06/>32 (77)	2/>16 (45)	2/>16 (64)
Clostridium spp.[f] (20)	0.03/1 (100)	0.125/4 (100)	≤0.06/0.5 (100)	1/8 (80)	0.25/16 (80)	0.5/8 (80)
Finegoldia magna (110)	0.06/0.125 (100)	≤0.06/0.125 (100)	0.125/0.25 (100)	0.5/8 (81)	8/>16 (40)	2/16 (64)
Peptoniphilus asaccharolyticus (40)	≤0.015/0.125 (100)	≤0.06/0.125 (100)	≤0.06/0.25 (100)	0.25/>32 (78)	4/>16 (35)	0.5/16 (78)
Miscellaneous gram-positive cocci[g] (77)	0.06/0.25 (100)	≤0.06/0.5 (100)	≤0.06/0.25 (100)	0.125/4 (90)	4/>16 (62)	1/16 (82)
Miscellaneous gram-positive rods[h] (49)	0.06/0.5 (100)	≤0.06/4 (96)	≤0.06/0.5 (100)	≤0.06/>32 (84)	0.5/8 (80)	0.5/4 (88)

[a] ETP, ertapenem; P/T, piperacillin-tazobactam; A/C, amoxicillin-clavulanic acid; CM, clindamycin; LVX, levofloxacin; MXF, moxifloxacin.

[b] *Bacteroides caccae* (*n* = 2), *B. distasonis* (*n* = 1), *B. fragilis* (*n* = 19), *B. ovatus* (*n* = 7), *B. stercoris* (*n* = 4), *B. thetaiotaomicron* (*n* = 8), *B. uniformis* (*n* = 5), and *B. vulgatus* (*n* = 5).

[c] *Fusobacterium nucleatum* (*n* = 7) and *Fusobacterium varium* (*n* = 3).

[d] *Porphyromonas asaccharolytica* (*n* = 30), *P. somerae* (*n* = 21), *P. catoniae* (*n* = 1), and *P. endodontalis* (*n* = 1).

[e] *Prevotella bivia* (*n* = 29), *P. corporis* (*n* = 6), *P. disiens* (*n* = 5), *P. enoeca* (*n* = 1), *P. intermedia* (*n* = 3), *P. melaninogenica* (*n* = 11), *P. oralis* (*n* = 1) *P. oris* (*n* = 2), *P. pallens* (*n* = 1), *P. tannerae* (*n* = 2), *P. veroralis* (*n* = 1), and *Prevotella* spp. (*n* = 4).

[f] *Clostridium aminovalericum* (*n* = 1), *C. cadaveris* (*n* = 4), *C. clostridioforme* (*n* = 3), *C. innocuum* (*n* = 1), *C. malenominatum* (*n* = 1), *C. perfringens* (*n* = 6), *C. septicum* (*n* = 1), *C. sphenoides* (*n* = 1), and *C. subterminale* (*n* = 2).

[g] *Peptostreptococcus anaerobius* (*n* = 15), *Peptostreptococcus micros* (*n* = 7), *Peptoniphilus harei* (*n* = 4), *Peptoniphilus indolicus* (*n* = 1), *Peptoniphilus ivorii* (*n* = 1), *Peptoniphilus lacrimalis* (*n* = 1), *Anaerococcus prevotii* (*n* = 14), *Anaerococcus octavius* (*n* = 1), *Anaerococcus tetradius* (*n* = 9), *Anaerococcus vaginalis* (*n* = 7), *Gemella morbillorum* (*n* = 3), *Ruminococcus productus* (*n* = 1), and anaerobic gram-positive cocci (*n* = 13).

[h] *Eubacterium lentum* (*n* = 1), *Eubacterium limosum* (*n* = 1), *Eubacterium nodatum* (*n* = 1), *Eubacterium saburreum* (*n* = 1), *Eubacterium* spp. (*n* = 13), *Propionibacterium acnes* (*n* = 19) *Propionibacterium* sp. (*n* = 1), *Actinomyces meyeri* (*n* = 1), *Actinomyces odontolyticus* (*n* = 1), *Actinomyces turicensis* (*n* = 1), *Arcanobacterium pyogenes* (*n* = 1), *Corynebacterium* CDC group G-like (anaerobic) (*n* = 2), *Lactobacillus brevis* (*n* = 1), *Lactobacillus casei* (*n* = 1), *Lactobacillus plantarum* (*n* = 2), *Lactobacillus uli* (*n* = 1), and an unusual gram-positive bacillus (*n* = 1).

(5.5 and 2.1 per specimen positive for anaerobes, respectively). This was particularly true for *Porphyromonas* species (70% and 23%, respectively), especially *Porphyromonas asaccharolytica* and *Porphyromonas somerae*, and *Prevotella* species (72% and 23%, respectively). In contrast, the anaerobic cocci and *B. fragilis* group isolates appeared to be about evenly distributed among all three specimen types. Among the aerobic organisms, MRSA and *Enterococcus faecalis* were isolated proportionately more frequently from swab specimens than from other specimens, while certain CoNS (*S. haemolyticus*, *S. lugdunensis*, and *S. simulans*) and *C. striatum* were isolated proportionately more frequently from tissue. Other aerobic organisms were evenly distributed. Half of the tissue specimens in our study contained anaerobes. This result differs from the results of a large clinical trial that found fewer anaerobes but that had enrolled patients with relatively mild infections who were not hospitalized (22).

We isolated relatively few aerobic gram-negative rods from our wound swab cultures, although six of our specimens (four from tissue specimens) had these exclusively, including three in pure culture. Several investigators have noted a higher prevalence of gram-negative rods and anaerobes in more severe infections than in milder ones (40, 45, 51). In our study, *P. aeruginosa* was isolated from 8.6% of the patients, but specimens from only 5.7% of the patients grew *P. mirabilis*, perhaps because of the requirement for effective wound debridement before specimen collection. Members of the family *Enterobacteriaceae* were mostly susceptible to the antimicrobial agents tested. The resistance of *S. maltophilia* has been noted previously (21).

Anaerobes, when they were present, were almost always present in mixed culture. The predominant organism was *F. magna*, which was isolated from 37.4% of the patients, often along with *S. aureus*. This is in contrast to the findings of several other studies (3, 17), which failed to isolate anaerobic gram-positive cocci in general, possibly because of the use of suboptimal collection or transport methods or because media selective for gram-positive anaerobes are not used by many laboratories. Brucella agar with laked blood, kanamycin, and vancomycin agar, the most frequently used selective anaerobe medium, grows *B. fragilis* group and *Prevotella* species but not gram-positive anaerobes, which could explain why many studies find *B. fragilis* group to be the predominant anaerobe isolated.

Porphyromonas species are slow growing and fastidious and thus are not as easily cultured as other anaerobes, which may explain why several studies did not report the isolation of either *Porphyromonas* species or *Prevotella* species among their gram-negative anaerobes (23). Some studies (45, 51) noted *Clostridium* species as a predominant organism from DFIs, whereas we isolated *Clostridium* species from only 4.9% of patients. Members of the *B. fragilis* group were present in 8.4% of the patients, with more than one species present in 11 patients.

MRSA has been a pathogen of concern in patients with DFIs for almost two decades. In fact, the first two isolates of vancomycin-resistant MRSA strains were from diabetic patients with foot lesions (8). More recently, the emergence of community-acquired MRSA has been noted (16, 37). In our study, cultures of specimens from 48 patients (11.8%) grew

MRSA, and 10 of these were in pure culture. Should this trend accelerate, it might further affect the choice of empirical antimicrobial therapy. We found the MRSA isolates to be generally susceptible to doxycycline (MIC_{90}s $\leq$ 2 μg/ml) and trimethoprim-sulfamethoxazole (MIC_{90}s $\leq$ 0.5/9.5 μg/ml) but resistant to clindamycin (MIC_{50}s $>$ 8 μg/ml). All strains were susceptible to vancomycin, linezolid, and daptomycin.

In cases in which MRSA was not found in pure culture, 57.9% (22 of 38) of those patients were also found to harbor anaerobes; 80% of these were gram-positive cocci, sometimes (10 of 22) as the sole anaerobic organism and other times along with pigmented *Prevotella* or *Porphyromonas* spp. or members of the *B. fragilis* group. In contrast, *E. faecalis*, found in 31.5% of the patients, was more often (80 of 138 cases) isolated in cultures with no anaerobic organisms. Predominant aerobes found with *E. faecalis* in these cultures were *S. aureus*, including MRSA; CoNS, particularly *S. epidermidis* and *S. haemolyticus*; and *P. aeruginosa*. Other frequent combinations seen were *S. epidermidis* in combination with *C. amycolatum* and other resistant corynebacteria and *S. aureus* in combination with *S. agalactiae* and other streptococci.

Our study demonstrates the large number and variety of organisms that can be isolated from properly obtained specimens that are optimally processed. While many factors must be considered, including previous antibiotic therapy, knowledge of the usual causative organisms in these infections and their antibiotic susceptibilities will allow clinicians to make informed choices. Certainly, empirical antibiotic therapy should include coverage for oxacillin-susceptible *S. aureus* or for MRSA in a patient with risk factors for infection with this pathogen. Because specimens from most patients with more than mild infections have polymicrobial cultures, empirical therapy should be relatively broad spectrum, especially for patients with severe infections and those who are immunocompromised. The antimicrobial susceptibility data from our study suggest that ertapenem or piperacillin-tazobactam would be appropriate single agents for empirical coverage (except for MRSA). Because of the high rates of resistance among staphylococci and anaerobic organisms, the use of fluoroquinolones alone might be inadequate and infections with these organisms may require additional antimicrobial coverage. The previously recommended combinations with clindamycin might be of limited efficacy, since 18% of anaerobes tested were resistant to clindamycin.

We encourage clinicians to obtain proper, postdebridement specimens for culture and urge clinical microbiology laboratories to report all organisms, at least to the genus level, recovered from such specimens. Reports of "normal cutaneous flora" or "no *S. aureus* isolated" are not helpful for properly collected specimens. Also, if necrotic tissue swabs are submitted, laboratories should not be expected to waste time and resources working up organisms of questionable etiologic importance. However, susceptibility testing should be performed routinely for staphylococci and gram-negative rods with unpredictable resistance. Other organisms may be tested selectively. We also hope that clinicians will use these reported culture and susceptibility results to help tailor their antimicrobial treatment choices.

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