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Comparative Activities of Cefuroxime, Amoxicillin-Clavulanic Acid, Ciprofloxacin, Enoxacin, and Ofloxacin against Aerobic and Anaerobic Bacteria Isolated from Bite Wounds

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We studied the comparative in vitro activities of 10 oral antimicrobial agents against 147 aerobic and 61 anaerobic bacteria making up species in 13 genera (*Staphylococcus aureus*, streptococci, *Eikenella corrodens*, *Pasteurella multocida*, *Haemophilus-Actinobacillus* spp., M-5, EF-4, *Moraxella* spp., *Flavobacterium* IIb, *Bacteroides melaninogenicus*, *Bacteroides* spp., *Fusobacterium* spp., and *Peptostreptococcus* spp.) that were isolated from bite wounds. Cefuroxime was generally >fourfold more active than cephalexin and cefadroxil against all aerobic isolates, including *Pasteurella multocida*. The fluoroquinolones were highly active against most aerobic isolates but were less active against anaerobic isolates. Ciprofloxacin was generally more active than either enoxacin or ofloxacin. Discrepancies of >30% in the interpretation of susceptibilities between break points suggested by the National Committee for Clinical Laboratory Standards and those related to oral dose peak levels (one-half to one-quarter of maximum achievable concentrations) were noted in 14% (18 of 130) of the instances.

The choice of an appropriate antimicrobial regimen for infections caused by animal and human bites poses a dilemma for clinicians. Approximately 80% of bite wounds harbor potential pathogens, including many unusual and fastidious aerobic and anaerobic bacteria (10). Anaerobic bacteria can be isolated from approximately 30 and 60% of animal and human bite wounds, respectively (2, 6, 7, 10), and their isolation has been associated with more severe clinical infections (11). Yet, in an era of cost-consciousness, these wounds are often not cultured aerobically and are rarely cultured anaerobically except in research studies. To compound these problems, most clinical laboratories are unable to determine the in vitro susceptibilities of fastidious aerobic and anaerobic bacteria that are frequently isolated from bite wounds.

Consequently, clinicians must sometimes rely on the medical literature to guide therapeutic choices, both empiric and specific. Only two systematic susceptibility studies with large numbers and varieties of bite pathogens exist in the English language literature (2, 9). In these studies both a high percentage of β-lactamase-producing bacteria (2) and the emergence of bacteria that are resistant to commonly used antimicrobial agents have been noted in several genera of isolates obtained from bite wounds (9). Information about newer alternative therapeutic agents and their in vitro activities against the full spectrum of species isolated from bite wounds is therefore needed to help guide clinicians.

Cefuroxime axetil, the new orally administered, esterified formulation of cefuroxime, and ciprofloxacin, an oral fluoroquinolone antibacterial agent, have recently been approved for use in skin and soft tissue infections. Ofloxacin and enoxacin are two other oral fluoroquinolones under investigation that have potential use in skin and soft tissue infections. Since these agents can be used to treat animal and human bite wound infections, we determined the comparative susceptibilities of 147 aerobic and 61 anaerobic bite wound isolates to these new antimicrobial agents and compared their activities with the activities of the older antimicrobial agents that are frequently used to treat bite wound infections.

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MATERIALS AND METHODS

All bacteria studied were clinical isolates and were identified by standard criteria (1, 13, 14, 17). The sources and numbers of isolates were as follows: dog bites, 81; cat bites, 33; human bites, 53; other animal bites, 4; and bites of unknown origin, 20. Eighteen *Flavobacterium* IIb isolates came from the collection of John M. Pickett (University of California, Los Angeles) and were from unknown clinical sources. The numbers and species of the isolates tested are given in Tables 1 and 2.

The following standard laboratory powders were supplied by the indicated companies: penicillin and cephalexin, Eli Lilly & Co., Indianapolis, Ind.; ampicillin, Bristol Laboratories, Syracuse, N.Y.; tetracycline, Pfizer Inc., New York, N.Y.; amoxicillin-clavulanic acid, Beecham Laboratories, Bristol, Tenn.; cefadroxil, Mead Johnson, Evansville, Ind.; cefuroxime, Glaxo Inc., Research Triangle Park, N.C.; ciprofloxacin, Miles Pharmaceuticals, West Haven, Conn.; ofloxacin, Ortho Pharmaceuticals Co., Raritan, N.J.; and enoxacin, Warner Lambert Co., Ann Arbor, Mich.

Strains were taken from frozen stock cultures and transferred twice to ensure purity and good growth. Aerobic bacteria were tested by standard procedures by the appropriate methods for the particular organism (9, 14). Mueller-Hinton agar supplemented with hemin (10 μg/ml) was the basal medium used for all aerobic isolates. The media for *Eikenella corrodens* and the viridans group streptococci were supplemented with 5% sheep blood, while media for *Haemophilus* spp., *Actinobacillus* spp., and II-J were supplemented with 5% rabbit blood. Anaerobic bacteria were cultured and inocula were prepared by the methods outlined in the *Wadsworth Anaerobic Bacteriology Manual* (17). Brucella agar supplemented with hemin, vitamin K_1, and 5%

TABLE 1. Comparative susceptibilities of aerobic human and animal bite wound isolates to cefuroxime, amoxicillin-clavulanic acid, ciprofloxacin, enoxacin, and ofloxacin

Organism (no.)	Antibacterial agent	MIC (μg/ml)[a]			% Susceptible at the break point (μg/ml)	
		Range	50%	90%	NCCLS	Oral dose-related
Staphylococcus aureus (20)	Cefuroxime	0.125–2.0	1.0	2.0	100 (8)	100 (2)
	Cephalexin	1.0–4.0	4.0	4.0	100 (8)	25[b] (2)
	Cefadroxyl	1.0–4.0	4.0	4.0	100 (8)	20[b] (2)
	Penicillin G	≤0.03–16	1.0	8.0	15 (≤0.1)	15 (≤0.1)
	Amoxicillin-clavulanic acid	≤0.03–1.0	0.5	1.0	100 (4, 2[c])	100 (4, 2[c])
	Ampicillin	≤0.03–8.0	2.0	4.0	20 (<0.2)	20 (<0.2)
	Tetracycline	0.25–64	0.5	32	85 (4)	85 (2)
	Ciprofloxacin	0.25–0.5	0.5	0.5	100 (1)	100 (1)
	Ofloxacin	0.125–0.5	0.25	0.5	100 (2)	100 (2)
	Enoxacin	0.5–2.0	1.0	2.0	100 (2)	100 (2)
Eikenella corrodens (17)	Cefuroxime	1.0–16	8.0	8.0	71 (8)	6[b] (2)
	Cephalexin	8.0–128	32	64	6 (8)	0 (2)
	Cefadroxyl	16.0–128	64	128	0 (8)	0 (2)
	Penicillin G	0.12–2.0	1.0	2.0	94 (2)	94 (2)
	Amoxicillin-clavulanic acid	0.12–1.0	1.0	1.0	100 (8, 4)	100 (4, 2)
	Ampicillin	0.25–4.0	0.5	2.0	88 (2)	88 (2)
	Tetracycline	2.0–8.0	2.0	8.0	88 (4)	7[b] (2)
	Ciprofloxacin	≤0.03–0.06	≤0.03	0.06	100 (1)	100 (1)
	Ofloxacin	≤0.03–0.125	0.06	0.06	100 (2)	100 (2)
	Enoxacin	0.06–0.5	0.06	0.5	100 (2)	100 (2)
Pasteurella multocida (20)	Cefuroxime	≤0.03–0.25	0.125	0.25	100 (8)	100 (2)
	Cephalexin	0.25–4.0	4.0	4.0	100 (8)	40[b] (2)
	Cefadroxyl	0.5–16	4.0	8.0	85 (8)	5[b] (2)
	Penicillin G	≤0.03–0.125	0.125	0.125	100 (2)	100 (1)
	Amoxicillin-clavulanic acid	≤0.03–0.5	0.125	0.25	100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–0.25	0.125	0.25	100 (2)	100 (2)
	Tetracycline	0.25–1.0	0.5	0.5	100 (4)	100 (2)
	Ciprofloxacin	≤0.03	≤0.03	<0.03	100 (1)	100 (1)
	Ofloxacin	≤0.03–0.25	≤0.03	0.06	100 (2)	100 (2)
	Enoxacin	<0.03–0.5	0.12	0.5	100 (2)	100 (2)
Haemophilus-Actinobacillus spp. (14)	Cefuroxime	0.06–2.0	0.25	2.0	100 (8)	100 (2)
	Cephalexin	0.5–16	4.0	8.0	93 (8)	36[b] (2)
	Cefadroxyl	0.25–16	8.0	16	64 (8)	14[b] (2)
	Penicillin G	0.06–0.5	0.25	0.5	100 (2)	100 (1)
	Amoxicillin-clavulanic acid	0.06–0.5	0.25	0.5	100 (4, 2)	100 (4, 2)
	Ampicillin	0.06–0.5	0.25	0.5	100 (2)	100 (2)
	Tetracycline	0.5–4.0	2.0	4.0	100 (4)	71[b] (2)
	Ciprofloxacin	≤0.03–0.06	≤0.03	0.06	100 (1)	100 (1)
	Ofloxacin	≤0.03–0.25	0.06	0.06	100 (2)	100 (2)
	Enoxacin	≤0.03–1.0	0.12	0.5	100 (2)	100 (2)
M-5 (10)	Cefuroxime	0.5–1.0	0.5	0.5	100 (8)	100 (2)
	Cephalexin	4.0	4.0	4.0	100 (8)	0[b] (2)
	Cefadroxyl	4.0–8.0	4.0	8.0	50 (8)	0[b] (2)
	Penicillin G	0.125–0.25	0.25	0.25	100 (2)	100 (1)
	Amoxicillin-clavulanic acid	0.125–0.25	0.125	0.25	100 (8, 4)	100 (4, 2)
	Ampicillin	0.125–0.25	0.125	0.25	100 (2)	100 (2)
	Tetracycline	0.5–0.5	0.5	0.5	100 (4)	100 (2)
	Ciprofloxacin	≤0.03	≤0.03	≤0.03	100 (1)	100 (1)
	Ofloxacin	≤0.03	≤0.03	≤0.03	100 (2)	100 (2)
	Enoxacin	0.12	0.12	0.12	100 (2)	100 (2)
EF-4 (13)	Cefuroxime	0.25–16.0	0.5	16	77 (8)	77 (2)
	Cephalexin	2.0–16.0	4.0	16	69 (8)	15[b] (2)
	Cefadroxyl	2.0–8.0	4.0	8.0	100 (8)	8[b] (2)
	Penicillin G	0.125–2.0	0.125	2.0	100 (2)	92 (1)
	Amoxicillin-clavulanic acid	0.125–0.5	0.25	0.5	100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–1.0	0.125	0.5	100 (2)	100 (2)
	Tetracycline	0.5–4.0	0.5	2.0	100 (4)	85 (2)
	Ciprofloxacin	≤0.03–0.6	≤0.03	0.06	100 (1)	100 (1)
	Orfloxacin	≤0.03–0.6	≤0.03	0.06	100 (2)	100 (2)
	Enoxacin	0.06–0.25	0.06	0.25	100 (2)	100 (2)

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TABLE 1–*Continued*

Organism (no.)	Antibacterial agent	MIC (μg/ml)[a]			% Susceptible at the break point (μg/ml)	
		Range	50%	90%	NCCLS	Oral dose-related
Streptococcus spp. (26)	Cefuroxime	≤0.03–2.0	0.25	2.0	100 (8)	100 (2)
	Cephalexin	0.06–16	4.0	8.0	96 (8)	19[b] (2)
	Cefadroxyl	0.06–8.0	4.0	8.0	100 (8)	19[b] (2)
	Penicillin G	≤0.03–0.25	0.06	0.12	96 (≤0.1)	96 (≤0.1)
	Amoxicillin-clavulanic acid	≤0.03–1.0	0.06	0.12	100 (4, 2)	100 (4, 2)
	Ampicillin	≤0.03–0.25	0.06	0.12	96 (≤0.1)	96 (≤0.1)
	Tetracycline	0.25–32	0.5	16	73 (4)	73 (2)
	Ciprofloxacin	0.25–8.0	1.0	4.0	58 (1)	58 (1)
	Ofloxacin	0.25–4.0	1.0	4.0	73 (2)	73 (2)
	Enoxacin	4.0–32	8.0	32	0 (2)	0 (2)
Moraxella spp. (6)	Cefuroxime	0.06–8.0	0.125		100 (8)	83 (2)
	Cephalexin	0.25–8.0	4.0		83 (8)	33[b] (2)
	Cefadroxyl	0.125–4.0	4.0		100 (8)	33[b] (2)
	Penicillin G	≤0.03–4.0	0.06		83 (2)	83 (1)
	Amoxicillin-clavulanic acid	≤0.03–1.0	0.125		100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–2.0	0.06		100 (2)	100 (2)
	Tetracycline	0.5–4.0	0.5		100 (4)	83 (2)
	Ciprofloxacin	≤0.03–0.25	≤0.03		100 (1)	100 (1)
	Ofloxacin	≤0.03–0.125	≤0.03		100 (2)	100 (2)
	Enoxacin	0.12–0.5	0.12		100 (2)	100 (2)
Flavobacterium IIB (18)	Cefuroxime	1–>128	>128	>128	6 (8)	6 (2)
	Cephalexin	8–>128	>128	>128	6 (8)	0 (2)
	Cefadroxyl	8–>128	>128	>128	6 (8)	0 (2)
	Penicillin G	2–>128	>128	>128	6 (2)	0 (1)
	Amoxicillin-clavulanic acid	1.0–32	32	32	11 (8, 4)	6 (4, 2)
	Ampicillin	1.0–>128	>128	>128	6 (2)	6 (2)
	Tetracycline	4.0–32	16.0	32	29 (4)	0 (2)
	Ciprofloxacin	0.5–1.0	0.5	0.5	100 (1)	100 (1)
	Ofloxacin	0.25–2.0	0.25	1.0	100 (2)	100 (2)
	Enoxacin	0.5–4.0	1.0	2.0	94 (2)	94 (2)

[a] MICs for 50 and 90% of isolates tested are indicated.
[b] Discrepancy of ≥30% between NCCLS and oral dose-related break points.
[c] First and second values are for amoxicillin and clavulanic acid, respectively.

laked sheep blood was the basal medium used for anaerobic isolates.

The plates were inoculated with a Steers replicator (Craft Machine Inc., Chester, Pa.). The inoculum used for aerobic bacteria was 10^4 CFU per spot, and the inoculum used for anaerobic bacteria and *Eikenella corrodens* was 10^5 CFU per spot. Control plates without antimicrobial agents were inoculated before and after each series of drug-containing plates were inoculated. Care was taken to avoid drug carry-over for the fluoroquinolones tested. Plates with aerobic isolates were incubated at 35°C in an aerobic environment for 24 h and were then examined. *Eikenella corrodens*, viridans group streptococci, *Haemophilus* spp., *Actinobacillus* spp., and II-J were incubated in 5 to 10% CO_2 for 48 h and were then examined. Anaerobic bacteria were incubated for 48 h in jars (GasPak; BBL Microbiology Systems, Cockeysville, Md.) and were then examined. Control strains of *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Streptococcus faecalis* ATCC 29212, *Bacteroides thetaiotaomicron* ATCC 29741, *Bacteroides fragilis* ATCC 25285, and *Eikenella corrodens* ATCC 23834 were tested simultaneously with the appropriate plates and environments.

RESULTS

The results of this study are summarized in Tables 1 and 2. In addition to reporting the MICs for 50 and 90% of strains tested for each species, we also report the percentage of isolates that were susceptible at the National Committee for Clinical Laboratory Standards (NCCLS) recommended break point (R. N. Jones, Antimicrob. Newsl. **31**:1–8, 1986) and at a break point representing one-half to one-quarter of the achievable peak concentrations in serum following a usual maximum oral dose of the antimicrobial agent (14, 15). Discrepancies between the two break points occurred with some drugs, because the NCCLS standards are often based on levels of an agent that are achieved after parenteral administration, and we were interested in the levels that related to oral doses since most bite wounds are treated with oral antimicrobial agents. A total of 18 (14%) discrepancies of >30% in the interpretation of the susceptibilities of isolates are indicated in Tables 1 and 2.

On a weight basis, cefuroxime was generally >fourfold more active than cephalexin and cefadroxil against all aerobic isolates (8 of 10 species), except for *Flavobacterium* IIb isolates, for which the MICs of all three cephalosporin

TABLE 2. Comparative susceptibilities of anaerobic human and animal bite wound isolates to cefuroxime, amoxicillin-clavulanic acid, ciprofloxacin, enoxacin, and ofloxacin

Organism (no.)	Antibacterial agent	MIC (μg/ml)[a]			% Susceptible at the break point (μg/ml)	
		Range	50%	90%	NCCLS	Oral dose-related
Bacteroides melaninogenicus group (16)	Cefuroxime	≤0.03–8.0	0.06	8.0	100 (8)	69[b] (2)
	Cephalexin	≤0.03–2.0	0.5	2.0	100 (8)	100 (2)
	Cefadroxyl	0.06–0.5	0.5	0.5	100 (8)	100 (2)
	Penicillin G	≤0.03–8.0	≤0.03	8.0	75 (2)	69 (1)
	Amoxicillin-clavulanic acid	≤0.03–0.25	≤0.03	0.12	100 (8, 4[c])	100 (4, 2[c])
	Ampicillin	0.06–4.0	0.06	4.0	88 (2)	88 (2)
	Tetracycline	0.125–32	0.5	4.0	94 (4)	88 (2)
	Ciprofloxacin	0.06–2.0	0.25	1.0	94 (1)	94 (1)
	Ofloxacin	0.125–2.0	0.5	2.0	100 (2)	100 (2)
	Enoxacin	0.25–16	4.0	8.0	19 (2)	19 (2)
Bacteroides spp. (17)	Cefuroxime	0.06–32	0.25	32	94 (8)	88 (2)
	Cephalexin	0.5–16	2.0	8.0	94 (8)	76 (2)
	Cefadroxyl	0.5–8.0	1.0	8.0	100 (8)	88 (2)
	Penicillin G	≤0.03–32	0.12	8.0	88 (2)	82 (1)
	Amoxicillin-clavulanic acid	≤0.03–0.5	0.06	0.5	100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–16	0.06	8.0	88 (2)	88 (2)
	Tetracycline	0.25–64	0.5	16	82 (4)	82 (2)
	Ciprofloxacin	0.06–32	1.0	2.0	82 (1)	82 (2)
	Ofloxacin	0.25–16	1.0	2.0	94 (2)	94 (2)
	Enoxacin	2.0–32	8.0	16	12 (2)	12 (2)
Fusobacterium spp. (18)	Cefuroxime	≤0.03–0.5	0.25	0.5	100 (8)	100 (2)
	Cephalexin	0.06–2.0	0.25	1.0	100 (8)	100 (2)
	Cefadroxyl	0.06–2.0	0.5	2.0	100 (8)	100 (2)
	Penicillin G	≤0.03–1.0	0.06	0.5	100 (2)	100 (1)
	Amoxicillin-clavulanic acid	≤0.03–0.12	0.06	0.12	100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–4.0	0.06	4.0	83 (2)	83 (2)
	Tetracycline	0.06–2.0	0.5	2.0	100 (4)	100 (2)
	Ciprofloxacin	0.25–32	2.0	32	33 (1)	33 (1)
	Ofloxacin	0.5–64	2.0	64	50 (2)	50 (2)
	Enoxacin	0.25–32	16	32	6 (2)	6 (2)
Peptostreptococcus spp. (10)	Cefuroxime	0.06–4.0	0.25	4.0	100 (8)	80 (2)
	Cephalexin	0.25–128	2.0	32	60 (8)	50 (2)
	Cefadroxyl	0.06–128	2.0	32	60 (8)	60 (2)
	Penicillin G	≤0.03–0.5	≤0.3	0.25	100 (2)	100 (1)
	Amoxicillin-clavulanic acid	≤0.03–1.0	0.06	0.5	100 (8, 4)	100 (4, 2)
	Ampicillin	≤0.03–1.0	0.06	0.5	100 (2)	100 (2)
	Tetracycline	0.25–64	1.0	32	60 (4)	50 (2)
	Ciprofloxacin	≤0.03–8.0	1.0	2.0	80 (1)	80 (1)
	Ofloxacin	≤0.03–8.0	1.0	4.0	80 (2)	80 (2)
	Enoxacin	0.125–32.0	4.0	8.0	20 (2)	20 (2)

[a] MICs for 50 and 90% of isolates tested are indicated.
[b] Discrepancy of ≥30% between NCCLS and oral dose-related break points.
[c] First and second values are for amoxicillin and clavulanic acid, respectively.

agents for 50% of strains tested were >128 μg/ml. Cefuroxime was active against all *Pasteurella multocida* isolates at a MIC of <0.25 μg/ml. Cephalexin and cephadroxil had MICs of 4 and 8 μg/ml, respectively, for 90% of strains tested. By using NCCLS break points, almost all *Pasteurella multocida* isolates were found to be susceptible to both agents; however, by using the oral break points, 60% of isolates were found to be resistant to cephalexin and 95% were found to be resistant to cefadroxil. Cefuroxime had activity comparable against anaerobic bacteria to those of cephalexin and cefadroxil, with the peptostreptococci showing the greatest percentage of resistance to all three cephalosporins.

The fluoroquinolones (ciprofloxacin, enoxacin, and ofloxacin) that were tested showed high degrees of activity against all aerobic isolates except for the streptococci, which were frequently resistant to all three fluoroquinolones. The fluoroquinolones were relatively less active against the anaerobic bacteria compared with their activity against the aerobic bacteria. Enoxacin was the least active fluoroquinolone, and a majority of all anaerobic isolates of all genera were resistant. Ciprofloxacin and ofloxacin had comparable activities. The fusobacteria were generally resistant to the fluoroquinolones.

Penicillin G was active against streptococci, EF-4, M-5, II-J, *Eikenella corrodens*, *Haemophilus-Actinobacillus* spp., and *Pasteurella multocida*. One strain of *Eikenella corrodens* and one strain of *Moraxella* sp. were relatively resistant to penicillin G, for both of which the MICs were 4 μg/ml. As expected, *Flavobacterium* IIb and *Staphylococcus aureus* isolates were generally resistant to penicillin G. Against the anaerobic bacteria tested, resistance to penicillin G was seen in 31% of the *Bacteroides melaninogenicus* group and 18%

of other non-*Bacteroides fragilis* species in the genus *Bacteroides*. The fusobacteria and peptostreptococci tested were all susceptible to penicillin G. Amoxicillin-clavulanic acid was active against all aerobic and anaerobic isolates at <1 μg/ml. It was not active against *Flavobacterium* IIb, which was generally resistant. Tetracycline was generally active against all aerobic genera and many of the anaerobic genera tested. The three strains of II-J tested (data not shown) were generally susceptible to all the agents tested.

DISCUSSION

While some clinicians advocate the use of oral cephalosporins such as cephalexin or cefadroxil for bite wounds (4), clinical failures are increasingly reported (5, 12, 18). Several in vitro studies, including this one, have noted a high percentage of resistance of bacterial species typically found in bite wounds (2, 8, 9, 16). Weber et al. (18) have noted that cephalexin and cefaclor do not achieve levels in blood that are sufficient to treat *Pasteurella multocida* infections reliably. In contrast, based on its in vitro activity against clinical isolates, cefuroxime appears to have potential clinical utility in the therapy of bite wounds. Cefuroxime was generally fourfold more active than cephalexin and cefadroxil, resulting in what should be inhibitory concentrations at a clinically achievable level. In mixed aerobic-anaerobic bite wound infections, either susceptibility studies should be performed when cefuroxime is used or clinical response should be watched carefully, since some anaerobic bacteria have been found to be resistant to cefuroxime.

In 18 of 130 (14%) instances, there were discrepancies of >30% in the susceptibility interpretation between the NCCLS criteria (Jones, Antimicrob. Newsl.) and those based on achievable oral levels of antimicrobial agents (14, 15). These occurred almost exclusively with the cephalosporins, particularly cephalexin and cefadroxil. Streptococci, *Haemophilus-Actinobacillus* spp., M-5, *Staphylococcus aureus*, *Moraxella* spp., EF-4, and *Pasteurella multocida* isolates were regarded as susceptible by NCCLS criteria and resistant by oral level criteria. This underscores the importance of creating separate break points for the oral and parenteral usage of antimicrobial agents. In support of this result is our own clinical experience, which has shown that the treatment of human bite wounds and clenched fist injuries with cephalexin may lead to therapeutic failure because of the presence of a combination of viridans group streptococci and *Eikenella corrodens* (5; unpublished data). Since cefuroxime was considerably more active than cephalexin and cefadroxil, there were only two instances, one with a strain of *Eikenella corrodens* and one with a strain of *Bacteroides melaninogenicus*, in which discrepancies were found.

The fluoroquinolones were generally very active against all aerobic isolates, including *Flavobacterium* IIb. However, they were deficient in their activities against aerobic streptococci. Streptococci are the bacteria that are most frequently isolated from bite wounds, usually in mixed cultures (10). Their role as synergistic pathogens with *Eikenella corrodens* has been documented (3), while their role either as primary pathogens or as synergistic pathogens with other species remains to be evaluated. The fluoroquinolones were also relatively inactive against many anaerobic bacteria. Consequently, their use in the treatment of bite wounds is also problematic and will require additional clinical evaluations.

Resistance to penicillin G was seen in seven genera, including 31% of the *Bacteroides melaninogenicus* and 18% of other *Bacteroides* spp. This confirms the data of Brook (2), who recovered β-lactamase-producing organisms in 41% (16 of 39) of cases, including 12 of 17 bite wounds treated with penicillin. Brook (2) has also noted that two of five *Bacteroides melaninogenicus* strains and one of three *Bacteroides oralis* strains that were isolated produced β-lactamases. Results of a previous study from our laboratory (9) noted that all the *Bacteroides* species isolated from animal bite wounds were penicillin susceptible, while 47% (7 of 15) isolated from human bite wounds produced β-lactamase and were penicillin resistant. In the present study, resistance of most anaerobic bacteria to penicillin G was found in human bite wound isolates; one *Bacteroides melaninogenicus* isolated from a cat bite wound produced β-lactamase and was penicillin resistant.

Amoxicillin-clavulanic acid has been shown to be clinically effective in the treatment of bite wound infections (11) and is considered by some to be the drug of choice for empiric therapy. Our in vitro data confirm its activity against almost all species of bacteria found in bite wounds. We did not encounter the development of any resistance to amoxicillin-clavulanic acid in bite wound isolates, despite its extensive use for the treatment of infections in these wounds. Only *Flavobacterium* IIb was resistant to amoxicillin-clavulanic acid.

Tetracycline had good in vitro activity against most isolates and, along with the expanded-spectrum agents of doxycycline and minocycline, offers potential utility as a therapeutic alternative in penicillin-allergic patients.

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