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Antimicrobial Susceptibilities of Anaerobic Bacteria Isolated from Female Genital Tract Infections

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Certain species or subspecies of anaerobic bacteria are isolated with higher frequency from female genital tract infections than from other anatomic sites. To gain susceptibility data more specific to the treatment of these infections, nine antimicrobial agents were tested by an agar dilution technique against 230 anaerobic bacteria isolated solely from obstetric and gynecological infections. These genital isolates were, in general, very susceptible to imipenem (most active, inhibiting all gram-negative rods at ≤1 μg/ml), clindamycin (all isolates inhibited at ≤4 μg/ml), metronidazole (all gram-negative rods inhibited at ≤4 μg/ml), and chloramphenicol. Penicillin G had generally low activity against *Bacteroides* spp., not restricted to just the *Bacteroides fragilis* group, although it was very active against gram-positive species. *Bacteroides bivius*, a species uniquely common in female genital infections, was particularly resistant (90% MIC, 64 U/ml). Also, the *Bacteroides melaninogenicus* isolates were less susceptible than previously reported for isolates not exclusively from genital sites. Compared with moxalactam, cefotaxime, and cefoperazone, cefoxitin usually demonstrated equal or greater activity against most *Bacteroides* spp., with the exception of greater activity of moxalactam against *B. fragilis* (formerly subsp. *fragilis*). Resistance to moxalactam was observed among strains of *Peptostreptococcus anaerobius*, a common genital isolate. Overall, the activities of these four drugs were not as predictable as those observed for clindamycin, metronidazole, chloramphenicol, and imipenem.

Anaerobic bacteria are recognized to be important pathogens in female genital tract infections, which frequently are polymicrobial in nature. With improvements in classification and methods of identification of anaerobic bacteria it is apparent that certain species, in particular *Bacteroides bivius*, *Bacteroides disiens*, *Gaffkya anaerobia*, and possibly *Peptostreptococcus anaerobius*, are somewhat unique to the female genital tract with regard to their higher frequency of isolation from both the endogenous flora (7) and from infection (5, 7) compared with the frequency of isolation from other body sites. Because of this, published data on the antimicrobial susceptibility of anaerobic bacteria, which encompass isolates from a wide spectrum of infections in which extragenital sites, e.g., respiratory or abdominal, are included or predominate may be only partially applicable to predicting the susceptibility of anaerobes from genital sites. Also in many previous reports of anaerobic susceptibility, test isolates have been combined into groups based on gram stain and morphology (e.g., anaerobic gram-positive cocci) or according to genus because of a limited number of isolates or incomplete identification or to simplify the presentation of data. Susceptibility data on such groups can be highly dependent on the relative proportions of member species included, which is not always stated. For these reasons, susceptibility tests were performed on a variety of gram-positive and gram-negative anaerobic bacteria isolated solely from obstetric and gynecological infections, and individual species have been delineated insofar as practicable to extend the information available on single species and to preclude combining species with quite different susceptibilities into a single group. These data on nine antimicrobial agents of interest for genital infections should provide more specific susceptibility data that can be applied to improve the choice of initial therapy to cover anaerobic bacteria.

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MATERIALS AND METHODS

Microorganisms. The anaerobic bacteria used for these susceptibility studies were cultured from infected patients admitted to the Obstetric and Gynecologic service of Duke University Medical Center. Patients from whom isolates were obtained for testing included 38 patients with endometritis after Caesarean section (21 patients), vaginal delivery (13 patients), or therapeutic or spontaneous abortion (4 patients) and 14 patients on the gynecology service diagnosed to have salpingitis (8 patients) with or without the presence of palpable masses or tubo-ovarian complexes as indicated by ultrasound, cuff infection after vaginal hysterectomy (3 patients), or pelvic abscess (3 patients). Patients in general had not received antibiotics within a 2-week period before culture, except for nine patients who had undergone Caesarean section and had received perioperative prophylactic antibiotic (usually cefazolin) or patients who had received therapy before operation for pelvic abscess. Specimens were obtained from one or more of the following sources, depending on the clinical setting: blood, pelvic abscess, cul-de-sac aspiration, abdominal wound, vaginal cuff, and endometrium. Culdocentesis was attempted in patients with the diagnosis of either endometritis or pelvic inflammatory disease. Where apparently identical isolates were cultured from different sites from the same patient, i.e., blood, cul-de-sac aspirate, and endometrium, only one of the multiple strains was selected for testing to avoid skewing the susceptibility data. The single strain was preferentially selected according to the specimen source in the same order as stated above. Endometrial isolates were given the lowest priority because of the possibility of contamination with endocervical flora during specimen collection. Pure cultures were maintained frozen at −70°C until inocula were prepared for susceptibility testing. The nomenclature of isolates was according to the *Anaerobe Laboratory Manual* (8).

Susceptibility tests were performed on 230 isolates; these generally reflect the anaerobic types and proportions that we isolate from obstetric and gynecological patients, with one exception. Only 19 strains belonging to the *Bacteroides fragilis* group were cultured from the 52 patients, and we wanted to test a larger number of these strains because of their significant pathogenicity and resistance to many antimicrobial agents. Thus, an additional 25 strains also isolated from genital tract infections were added, making the representation of *B. fragilis* group strains higher in proportion to other species than we usually observe.

Antimicrobial agents. Laboratory standard powders were kindly provided as follows: penicillin G and moxalactam from Eli Lilly & Co., Indianapolis, Ind.; cefoxitin and imipenem from Merck Sharp & Dohme, Rahway, N.J.; clindamycin from The Upjohn Co., Kalamazoo, Mich.; chloramphenicol from Parke, Davis & Co., Detroit, Mich.; metronidazole from G. D. Searle & Co., Chicago, Ill.; cefoperazone from Pfizer Pharmaceuticals, New York, N.Y.; and cefotaxime from Hoechst-Roussel Pharmaceuticals, Inc., Somerville, N.J. The drugs were stored as indicated by the manufacturers. Stock dilutions at 2,560 μg or units of active agent per ml were prepared in sterile distilled water or in the diluent recommended by the manufacturer, except for clindamycin, imipenem, and moxalactam which were diluted the day of a test. Drug dilutions were utilized within the appropriate time limits if specific recommendations were made by the manufacturer. Metronidazole powder, stock dilutions, and drug-containing plates were stored in the dark as recommended.

Susceptibility tests. The MIC was determined by using the proposed reference dilution procedure for antimicrobial susceptibility testing of anaerobic bacteria published by the National Committee for Clinical Laboratory Standards (14) with the following modifications, which were made to ensure that the more fastidious isolates could also be tested. For preparation of inocula, strains were cultured in thioglycolate (BBL Microbiology Systems, Cockeysville, Md.; no. 135-C) as recommended, except that vitamin K_1 was present at 1 μg/ml instead of 0.1 μg/ml and 10% inactivated rabbit serum was incorporated as an additional enrichment. Tween 80 (0.02%) was added to the thioglycolate for culture of gram-positive strains. Wilkins-Chalgren agar (Difco Laboratories, Detroit, Mich.) plates containing antimicrobial agents were dried for 45 to 60 min at 37°C in an ambient air incubator and then prestored for approximately 2 h, inoculated (Steers replicator), and incubated (37°C for 48 h) inside an anaerobic glove box (Coy Laboratory Products, Inc., Ann Arbor, Mich.) containing 85% N_2, 10% H_2, and 5% CO_2. Although the lot of Wilkins-Chalgren agar used supported adequate growth of all eight of the recommended growth control strains (14), certain strains of *Bacteroides* spp., particularly some *Bacteroides capillosus*, *Bacteroides asaccharolyticus*, *Bacteroides melaninogenicus*, and *B. bivius*, and *P. anaerobius* either did not grow or did not produce confluent growth on Wilkins-Chalgren medium during one or more runs. These organisms were successfully tested by incorporation of 5% lysed sheep blood in the Wilkins-Chalgren agar or the use of shorter incubation times (5 to 7 h) for preparation of the test inocula of organisms known to be rapid growers. The MIC endpoints also stayed within the acceptable MIC range for the three MIC reference strains, namely, *Clostridium perfringens* (ATCC 13124), *B. fragilis* (ATCC 25285), and *Bacteroides thetaiotaomicron* (ATCC 29741), on the occasions when 5% lysed sheep blood was added to the Wilkins-Chalgren medium.

The activities of these antimicrobial agents are presented as the MIC range and the lowest concentration of antimicrobial agent that inhibited at least 50 and 90% of the strains tested in a particular group (MIC_{50} and MIC_{90}, respectively). In this report stated comparisons of antimicrobial activities are generally based on the clinically achievable blood levels rather than on activity on a weight basis. Isolates have been considered susceptible or moderately susceptible if the MIC of the drug was less than or equal to the following breakpoints: penicillin G, 32 U/ml; chloramphenicol and metronidazole, 16 μg/ml; clindamycin and imipenem, 8 μg/ml; cefoxitin, moxalactam, cefoperazone, and cefotaxime, 32 μg/ml.

RESULTS AND DISCUSSION

Anaerobic gram-negative bacilli. Species of *Bacteroides* are the most frequently isolated among anaerobic bacteria, which are etiological in genital tract infections. Susceptibility tests were performed on 123 anaerobic gram-negative rods, mostly *Bacteroides* spp.; results with the major species and groups are detailed in Table 1. Clindamycin, metronidazole, chloramphenicol, and especially imipenem were the most active overall against strains of *Bacteroides* spp.; clindamycin was particularly effective against non-*B. fragilis* group *Bacteroides* spp. such as *B. bivius*. Interestingly, cefoxitin was generally more active than the third-generation cephalosporins tested. For these genital isolates, considerable resistance to penicillin G was demonstrated among other *Bacteroides* spp. in addition to that observed with the *B. fragilis* group.

B. bivius, which is the most frequently isolated species among anaerobic gram-negative bacilli from combined obstetric and gynecological infections in our hospital (5), demonstrated significant resistance to penicillin G (Table 1). Previously, we reported that 52% of *B. bivius* isolated from genital tract infections (5) were resistant to 2 U of penicillin G per ml, corresponding to ordinary doses. In the present study there were no *B. bivius* strains susceptible at 2 U/ml, and for some isolates the MIC of penicillin G exceeded the clinically achievable level, enhancing our impression of an increase in penicillin resistance among *B. bivius*. A high proportion of *B. bivius* isolates produce beta-lactamase (18).

In Table 1 the former subspecies of the *B. fragilis* group are presented separately as *B. fragilis*, *Bacteroides distasonis*, *Bacteroides ovatus*, *Bacteroides vulgatus*, and *B. thetaiotaomicron* since these species differed in their susceptibility patterns with certain antimicrobial agents (Table 1). Although penicillin had low activity for genital isolates of the *B. fragilis* group overall, the degree of resistance was not as great as has been reported previously, where probably abdominal isolates have been most represented (6, 19). It is interesting that in the present study isolates of *B. bivius* were approximately as resistant to penicillin G as *B. fragilis* and *B. thetaiotaomicron* and were more resistant than other *B. fragilis* group isolates. Among the third-generation cephalosporins and cefoxitin, moxalactam was most active against these genital isolates of *B. fragilis* (formerly subsp. *fragilis*). The former subspecies other than *B. fragilis*, taken collectively, were more susceptible to cefoxitin, which inhibited all isolates at 32 μg/ml, than to cefotaxime, moxalactam, and cefoperazone, which inhibited 76, 72, and 60% of isolates, respectively.

The black-pigmenting *Bacteroides* spp. comprise a heterogeneous group that previously were all called *Bacteroides melaninogenicus* and include in this text (Table 1) *B. melaninogenicus* (eight subsp. *intermedius* and one subsp. *levii*)

TABLE 1. Comparative activities of nine antimicrobial agents against genital tract isolates of anaerobic bacteria

Organism(s) (no. of strains)	Antibiotic	Range	MIC (μg/ml)	
			50%	90%
Bacteroides bivius (24)	Penicillin[a]	4.0–64	16	64
	Chloramphenicol	1.0–2.0	2	2
	Clindamycin	≤0.015–0.031	≤0.015	0.031
	Metronidazole	0.5–4.0	1	2
	Cefoxitin	≤0.062–8.0	2	4
	Moxalactam	≤0.062–32	8	16
	Cefoperazone	0.25–16	4	8
	Cefotaxime	≤0.062–32	4	16
	Imipenem	≤0.015–0.125	≤0.015	0.062
Bacteroides fragilis (16)	Penicillin	8.0–64	32	32
	Chloramphenicol	4.0	4	4
	Clindamycin	0.031–2.0	0.5	2
	Metronidazole	0.125–1.0	0.5	1
	Cefoxitin	4.0–32	8	32
	Moxalactam	0.5–16	0.5	4
	Cefoperazone	4.0–64	16	32
	Cefotaxime	2.0–32	8	16
	Imipenem	0.031–0.25	0.062	0.125
Bacteroides thetaiotaomicron (8)	Penicillin	32–64	32	64
	Chloramphenicol	4.0–8.0	8	8
	Clindamycin	0.062–4.0	4	4
	Metronidazole	0.25–1.0	0.5	1
	Cefoxitin	8.0–32	32	32
	Moxalactam	1.0–>64	32	>64
	Cefoperazone	32–64	64	64
	Cefotaxime	16–>64	32	>64
	Imipenem	0.062–0.5	0.25	0.5
Bacteroides vulgatus (7)	Penicillin	2.0–32		
	Chloramphenicol	2.0–8.0		
	Clindamycin	≤0.015–2.0		
	Metronidazole	0.25–1.0		
	Cefoxitin	2.0–32		
	Moxalactam	0.25–32		
	Cefoperazone	8.0–64		
	Cefotaxime	1.0–32		
	Imipenem	0.062–0.25		
Bacteroides distasonis (4)	Penicillin	8.0–16		
	Chloramphenicol	4.0–8.0		
	Clindamycin	0.062–4.0		
	Metronidazole	0.5		
	Cefoxitin	8.0–32		
	Moxalactam	8.0–>64		
	Cefoperazone	16–32		
	Cefotaxime	0.5–2.0		
	Imipenem	0.5–1.0		
Bacteroides ovatus (6)	Penicillin	8.0–32		
	Chloramphenicol	4.0–8.0		
	Clindamycin	1.0–2.0		
	Metronidazole	0.5–1.0		
	Cefoxitin	2.0–32		
	Moxalactam	1.0–>64		
	Cefoperazone	8.0–64		
	Cefotaxime	8.0–64		
	Imipenem	0.125–0.5		
Bacteroides melaninogenicus (9)	Penicillin	0.031–32	4	32
	Chloramphenicol	2.0–4.0	4	4
	Clindamycin	≤0.015–0.031	≤0.015	0.031
	Metronidazole	0.25–4.0	2	4
	Cefoxitin	≤0.062–4.0	0.5	4
	Moxalactam	0.125–8.0	0.25	8
	Cefoperazone	0.5–4.0	2	4
	Cefotaxime	≤0.062–8.0	0.25	8
	Imipenem	≤0.015–0.062	0.031	0.062

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TABLE 1—*Continued*

Organism(s) (no. of strains)	Antibiotic	Range	MIC (μg/ml)	
			50%	90%
Bacteroides asaccharolyticus (9)	Penicillin	≤0.015–8.0	0.25	8
	Chloramphenicol	≤0.25–4.0	1	4
	Clindamycin	≤0.015	≤0.015	≤0.015
	Metronidazole	≤0.062–1.0	0.125	1
	Cefoxitin	≤0.062–0.25	0.125	0.25
	Moxalactam	≤0.062–1.0	≤0.062	1
	Cefoperazone	≤0.062–0.5	≤0.062	0.5
	Cefotaxime	≤0.062–0.5	≤0.062	0.5
	Imipenem	≤0.015	≤0.015	≤0.015
Bacteroides capillosus (6)	Penicillin	0.125–64		
	Chloramphenicol	2.0–4.0		
	Clindamycin	≤0.015–0.031		
	Metronidazole	1.0–4.0		
	Cefoxitin	1.0–4.0		
	Moxalactam	0.5–64		
	Cefoperazone	4.0–16		
	Cefotaxime	0.125–32		
	Imipenem	0.031–0.062		
Bacteroides disiens (7)	Penicillin	0.062–32		
	Chloramphenicol	1.0–2.0		
	Clindamycin	≤0.015		
	Metronidazole	0.25–2.0		
	Cefoxitin	0.125–4.0		
	Moxalactam	0.25–16		
	Cefoperazone	1.0–8.0		
	Cefotaxime	0.125–16		
	Imipenem	≤0.015–0.062		
Bacteroides ruminicola (4)	Penicillin	1.0–32		
	Chloramphenicol	1.0–2.0		
	Clindamycin	≤0.015		
	Metronidazole	0.125–4.0		
	Cefoxitin	1.0–8.0		
	Moxalactam	2.0–32		
	Cefoperazone	0.5–4.0		
	Cefotaxime	0.25–4.0		
	Imipenem	0.031–0.062		
Bacteroides uniformis (4)	Penicillin	8.0–16		
	Chloramphenicol	0.5–4.0		
	Clindamycin	0.062–1.0		
	Metronidazole	0.25–0.5		
	Cefoxitin	2.0–4.0		
	Moxalactam	0.5–4.0		
	Cefoperazone	8.0–16		
	Cefotaxime	8.0–16		
	Imipenem	0.125–0.25		
Bacteroides spp. (6)	Penicillin	0.062–32		
	Chloramphenicol	1.0–8.0		
	Clindamycin	≤0.015–0.50		
	Metronidazole	0.125–2.0		
	Cefoxitin	0.5–8.0		
	Moxalactam	0.25–32		
	Cefoperazone	0.125–32		
	Cefotaxime	≤0.062–16		
	Imipenem	≤0.015–0.125		
Fusobacterium spp. (10)	Penicillin	≤0.015–2	0.125	1
	Chloramphenicol	≤0.25–2	1	1
	Clindamycin	≤0.015–1	0.062	0.25
	Metronidazole	≤0.062–4	0.125	0.25
	Cefoxitin	≤0.062–32	0.25	2
	Moxalactam	≤0.062–4	0.25	4
	Cefoperazone	≤0.062–16	0.25	4
	Cefotaxime	≤0.062–32	0.25	8
	Imipenem	≤0.015–0.25	0.062	0.25

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TABLE 1—*Continued*

Organism(s) (no. of strains)	Antibiotic	Range	MIC (μg/ml)	
			50%	90%
Peptostreptococcus anaerobius (22)	Penicillin	0.031–8.0	0.125	8
	Chloramphenicol	≤0.25–1.0	1	1
	Clindamycin	≤0.015–0.25	0.031	0.25
	Metronidazole	≤0.062–0.25	0.125	0.25
	Cefoxitin	0.125–16	0.25	8
	Moxalactam	0.25–>64	2	64
	Cefoperazone	≤0.062–16	1	8
	Cefotaxime	≤0.062–4.0	0.125	4
	Imipenem	≤0.015–1.0	0.031	0.5
Peptococcus asaccharolyticus (14)	Penicillin	≤0.015–0.25	≤0.015	0.25
	Chloramphenicol	≤0.25–2.0	1	2
	Clindamycin	0.062–0.50	0.125	0.50
	Metronidazole	0.5–1.0	0.5	1
	Cefoxitin	≤0.062–0.25	≤0.062	0.25
	Moxalactam	≤0.062–0.25	0.125	0.25
	Cefoperazone	≤0.062–0.25	0.125	0.25
	Cefotaxime	≤0.062–0.25	0.125	0.25
	Imipenem	≤0.015–0.031	≤0.015	≤0.015
Peptococcus magnus (5)	Penicillin	0.125		
	Chloramphenicol	2.0–4.0		
	Clindamycin	0.125–2.0		
	Metronidazole	1.0		
	Cefoxitin	0.125–0.25		
	Moxalactam	0.50–1.0		
	Cefoperazone	0.25–1.0		
	Cefotaxime	1.0–2.0		
	Imipenem	≤0.015–0.031		
Peptococcus spp. (8)	Penicillin	≤0.015–4.0	0.031	4
	Chloramphenicol	0.50–4.0	1	4
	Clindamycin	0.031–0.5	0.125	0.5
	Metronidazole	≤0.062–>32	≤0.062	>32
	Cefoxitin	≤0.062–4.0	≤0.062	4
	Moxalactam	≤0.062–64	0.50	64
	Cefoperazone	≤0.062–2.0	0.25	2
	Cefotaxime	≤0.062–1.0	≤0.062	1
	Imipenem	≤0.015–1.0	≤0.015	1
Gaffkya anaerobia (14)	Penicillin	≤0.015–0.5	≤0.015	0.5
	Chloramphenicol	1.0–4.0	2	4
	Clindamycin	0.031–2.0	0.25	1
	Metronidazole	0.5–2.0	0.5	1
	Cefoxitin	≤0.062–2.0	0.125	0.5
	Moxalactam	0.25–4.0	1	4
	Cefoperazone	≤0.062–8.0	≤0.062	2
	Cefotaxime	0.125–4.0	0.25	1
	Imipenem	≤0.015–0.062	≤0.015	0.062
Streptococcus spp. (8)	Penicillin	0.031–0.25	0.062	0.25
	Chloramphenicol	2.0–8.0	2	8
	Clindamycin	0.031–0.5	0.125	0.5
	Metronidazole	16–>32	>32	>32
	Cefoxitin	0.5–8.0	4	8
	Moxalactam	0.125–16	8	16
	Cefoperazone	≤0.062–0.25	0.25	0.25
	Cefotaxime	≤0.062–1.0	0.125	1
	Imipenem	≤0.015–0.062	≤0.015	0.062
Lactobacillus spp. (7)	Penicillin	0.125–0.5		
	Chloramphenicol	2.0–8.0		
	Clindamycin	≤0.015–0.062		
	Metronidazole	1.0–>32		
	Cefoxitin	0.25–32		
	Moxalactam	1.0–32		
	Cefoperazone	0.125–4.0		
	Cefotaxime	≤0.062–4.0		
	Imipenem	0.031–0.5		

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TABLE 1—*Continued*

Organism(s) (no. of strains)	Antibiotic	Range	MIC (μg/ml)	
			50%	90%
Bifidobacterium spp. (7)	Penicillin	≤0.015–0.5		
	Chloramphenicol	2.0–4.0		
	Clindamycin	≤0.015–0.062		
	Metronidazole	1.0–>32		
	Cefoxitin	0.125–32		
	Moxalactam	0.5–8.0		
	Cefoperazone	≤0.062–1.0		
	Cefotaxime	≤0.062–4.0		
	Imipenem	0.031–0.5		

[a] Penicillin MICs are given in units per milliliter.

and *B. asaccharolyticus*, a species formerly classified as *B. melaninogenicus* subsp. *asaccharolyticus*. No distinct differences in susceptibilities among members of the *B. melaninogenicus* group previously were noted in 1976 (19). Presently, however, these *B. melaninogenicus* subsp. *intermedius* strains were considerably less susceptible than *B. asaccharolyticus* strains to cefoxitin, moxalactam, cefoperazone, cefotaxime, metronidazole, and particularly to penicillin G, although all MIC_{90}s were still at or below the respective breakpoints. The high MIC_{90} of penicillin G with these genital tract isolates of *B. melaninogenicus* subsp. *intermedius* is notable. Even adding in the isolates of *B. asaccharolyticus* for comparison, since this subspecies was included among *B. melaninogenicus* in previous reports, only 67% of our isolates were susceptible to penicillin G at ≤2 U/ml compared with 83% in 1972 (12), 86% in 1976 (19), and 92% in 1980 (15). Yet, reported susceptibilities have, in general, been somewhat variable (1, 11, 12, 15, 19), and a number of investigators have concluded that resistance to penicillin G has increased among the *B. melaninogenicus* group (1, 13, 15). Differences may relate to other variables particular to a geographic locale, but a portion of this diversity in reported susceptibility data also may be based on different specimen sources and the fact that species or strains from different body sites are more dissimilar in their susceptibilities than previously appreciated. These female genital tract isolates were considerably less susceptible than isolates of which all or most were from the respiratory tract of both normal persons and infected patients (15).

Additional species of *Bacteroides*, including *B. capillosus*, *B. disiens*, *Bacteroides ruminicola*, *Bacteroides uniformis*, and unidentifiable *Bacteroides* spp. are common, taken collectively, in genital infections. These species were relatively resistant to penicillin G, particularly strains of *B. capillosus* and *B. disiens* (Table 1). The limited data (3, 9, 10, 17) available on these less well studied species of *Bacteroides* and some of these same antimicrobial agents are, in general, similar even when probably few strains were derived from female genital tract sites (10).

Fusobacterium gonidiaformans (four strains), *Fusobacterium naviforme* (two strains), *Fusobacterium nucleatum* (one strain), *Fusobacterium russii* (one strain), *Fusobacterium symbiosum* (one strain), and unidentifiable *Fusobacterium* spp. (one strain) are presented in combined fashion in Table 1 since most strains of *Fusobacterium* spp. were very susceptible to the nine antimicrobial agents. However, the MIC of cefotaxime for four strains was relatively high: one *F. symbiosum* (32 μg/ml), two *F. gonidiaformans* (8 μg/ml), and one *F. russii* (8 μg/ml). The same strain of *F. russii* also required 16 μg of cefoperazone per ml and 32 μg of cefoxitin per ml for inhibition. Thus, whereas the majority of *Fusobacterium* spp. strains have been highly susceptible to penicillin G, the activity of the newer cephalosporins against these exclusively genital isolates was not as predictable. Similar findings also have been reported for strains whose sources are for the most part unknown (2–4, 9, 11, 20).

Three additional isolates of anaerobic gram-negative bacilli, one *Bacteroides splanchnicus* and two unidentifiable strains, were within the susceptible range of these antimicrobial agents.

Anaerobic cocci. A total of 81 strains of anaerobic cocci were tested. Other than the species listed in Table 1, four strains of *Peptococcus prevotii* and four unidentifiable *Peptococcus* strains were combined (under *Peptococcus* spp.), as were strains of *Streptococcus* including *Streptococcus intermedius* (four strains), *Streptococcus morbillorum* (two strains), *Streptococcus constellatus* (one strain), and one unidentifiable *Streptococcus* sp. since the susceptibility patterns of these group members were similar. The strains of *Streptococcus* spp. were included with the anaerobes since some were isolated initially only under anaerobic conditions or preferred or required anaerobic conditions for growth even after subculture. Other isolates of anaerobic cocci not included in Table 1 were *Peptostreptococcus micros* (two strains), *Peptostreptococcus productus* (one strain), *Veillonella parvula* (three strains), and four unidentifiable strains, three of which were gram positive. These latter isolates were susceptible to all of the antimicrobial agents.

The anaerobic gram-positive cocci are very common in genital infections, but have not been considered a problem in therapy because of their generally high susceptibility to commonly used antimicrobial agents (except for aminoglycosides), including penicillin G and the older cephalosporins. Even though the newer cephalosporins and cefoxitin were less active than penicillin G, these drugs still should be generally quite effective considering the serum levels achieved. An exception for strains of *P. anaerobius*, which is one of the most frequent isolates from genital infections in our hospital, is possible, particularly with moxalactam. Of a total of 22 strains of *P. anaerobius*, the MIC of moxalactam was ≥8 μg/ml for nine strains, whereas the other strains had moxalactam MIC values of ≤2 μg/ml. Three strains for which the MIC of moxalactam was ≥64 μg/ml were, in addition, considerably less susceptible than the other strains to cefotaxime (MICs, 4 μg/ml) and to cefoperazone, cefoxitin, and penicillin G (MICs, 8 to 16 μg/ml or U/ml). A similar

tendency was observed among strains for which the MIC of moxalactam was 8 to 32 μg/ml. The influence of these strains is reflected in the higher MIC_{90} values for penicillin, cefoxitin, moxalactam, cefoperazone, and cefotaxime than usually expected for anaerobic cocci (Table 1), but the impact of this occasional resistance on therapy remains uncertain at present. In previous reports that usually have not delineated susceptibility by species or indicated the specific clinical sources, all isolates of anaerobic gram-positive cocci generally have been susceptible to these β-lactam antibiotics with relatively lower MIC_{90} levels (2, 3, 9, 17, 20) compared with these genital strains, except on occasion for moxalactam (6, 17). The resistance to metronidazole among microaerophilic or anaerobic streptococci rarely should create a problem in therapy since these organisms are isolated much less frequently from genital infections than are the obligately anaerobic strains of *Peptococcus* spp., *Gaffkya anaerobia*, and *Peptostreptococcus* spp.

Anaerobic gram-positive bacilli. The most frequently isolated genera of gram-positive bacilli were *Lactobacillus* and *Bifidobacterium* (Table 1). Strains combined under *Lactobacillus* spp. included *Lactobacillus jensenii* (two strains), *Lactobacillus brevis* (one strain), and *Lactobacillus minutus* (one strain) and three other strains that could not be identified to species. Combined strains of *Bifidobacterium* spp. included *Bifidobacterium breve* (two strains), *Bifidobacterium infantis* (one strain), *Bifidobacterium adolescentis* (one strain), and three unidentifiable species. The patterns of susceptibilities were similar for these two genera (Table 1). Other gram-positive bacilli isolated included *Propionibacterium acnes* (three strains), *Clostridium perfringens* (one strain), *Clostridium cadaveris* (one strain), *Clostridium innocuum* (one strain), *Clostridium difficile* (one strain), two unidentifiable strains of *Eubacterium* sp., one unidentifiable strain of *Actinomyces* sp., and two unidentifiable gram-positive bacilli. These organisms, except for *C. difficile*, generally were very susceptible to most of the antimicrobial agents, although *P. acnes* and one of the unidentifiable gram-positive strains were resistant to metronidazole. The strain of *C. difficile* was generally quite resistant, with MICs of cefoxitin, cefotaxime, cefoperazone and moxalactam at ≥64 μg/ml, whereas metronidazole was most active (MIC, 0.5 μg/ml).

Susceptibility data on the anaerobic gram-positive bacilli, particularly the non-spore-forming bacilli, has been limited, but does not appear to be different for these exclusively genital isolates. These organisms were very susceptible to the older beta-lactam antibiotics, but presently were less susceptible to these newer cephalosporins and cefoxitin, although they generally remain within a clinically applicable range. Resistance to metronidazole among strains of *Lactobacillus* spp., *Bifidobacterium* spp., *Propionibacterium* spp., and *Actinomyces* spp. also has been noted previously, although presently the single *Actinomyces* sp. isolate was susceptible. Yet, as indicated by the number of present strains studied, anaerobic gram-positive bacilli are not frequently isolated from genital infections (5), so that these exceptions may not have an adverse therapeutic impact, except in unusual settings.

In summary, these data on anaerobic isolates from the genital tract demonstrate that although certain patterns of susceptibility presently are highly predictable with regard to a group, genus, or species and a particular antimicrobial agent(s); in other instances there is a lack of predictability. This variability in susceptibility was particularly apparent with moxalactam, cefoperazone, cefotaxime, and cefoxitin, although cefoxitin was most often the more active compared with the third-generation cephalosporins. Yet, these agents, in general, lacked the high degree of activity or breadth of spectrum (or both) associated with clindamycin, chloramphenicol, metronidazole, and imipenem. These in vitro data support imipenem as an additional excellent candidate for therapy of serious pelvic infection. Penicillin G, on the other hand, demonstrated relatively poor activity overall against genital strains of *Bacteroides* spp., not only just the *B. fragilis* group, expressing substantial activity only against fusobacteria and gram-positive species. Similar results for some of the same species and antimicrobial agents which were obtained from endometrial wash specimens have been reported (16).

Further, we suggest that susceptibility data pertinent to infections in the genital tract may not necessarily be inferred correctly from data on anaerobic isolates from other body sites. Although the present data should be useful in attempting to anticipate effective antimicrobial agents for female genital infections, it is important to note other variables which might influence their effective application. These are as follows: changing susceptibility over time (apparent with penicillin G), differences in identification of genera or species, the degree of screening of clinical specimens employed to avoid endogenous flora, the proportion of isolates from patients who previously had received antimicrobial agents as prophylaxis or therapy, and the pattern of antibiotic usage in each hospital. These variables and others, such as the potential for plasmid-mediated transferrable resistance, point to the need for more readily available susceptibility testing for anaerobic bacteria in the individual hospital to assure the susceptibility of isolates from patients who are seriously ill or do not respond to empiric therapy.

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