SUPPLEMENT ARTICLE

# Lessons Learned from the Anaerobe Survey: Historical Perspective and Review of the Most Recent Data (2005–2007)

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***Background.*** The rationale and lessons learned through the evolution of the National Survey for the Susceptibility of *Bacteroides fragilis* Group from its initiation in 1981 through 2007 are reviewed here. The survey was conceived in 1980 to track emerging antimicrobial resistance in *Bacteroides* species.

***Methods.*** Data from the last 11 years of the survey (1997–2007), including 6574 isolates from 13 medical centers, were analyzed for in vitro antimicrobial resistance to both frequently used and newly developed antianaerobic agents. The minimum inhibitory concentrations of the antibiotics were determined using agar dilution in accordance with Clinical and Laboratory Standards Institute recommendations.

***Results.*** The analyses revealed that the carbapenems (imipenem, meropenem, ertapenem, and doripenem) and piperacillin-tazobactam were the most active agents against these pathogens, with resistance rates of 0.9%–2.3%. In the most recent 3 years of the survey (2005–2007), resistance to some agents was shown to depend on the species, such as ampicillin-sulbactam against *Bacteroides distasonis* (20.6%) and tigecycline against *Bacteroides uniformis* and *Bacteroides eggerthii* (~7%). Very high resistance rates (>50%) were noted for moxifloxacin and trovafloxacin, particularly against *Bacteroides vulgatus*. During that period of study, non–*B. fragilis Bacteroides* species had >40% resistance to clindamycin. Metronidazole-resistant *Bacteroides* strains were also first reported during that period.

***Conclusions.*** In summary, resistance to antibiotics was greater among non–*B. fragilis Bacteroides* species than among *B. fragilis* and was especially greater among species with a low frequency of isolation, such as *Bacteroides caccae* and *B. uniformis*. The emergence of resistance among the non–*B. fragilis Bacteroides* species underscores the need for speciation of *B. fragilis* group isolates and for clinicians to be aware of associations between species and drug resistance.

In 1980, Francis P. Tally and Sherwood L. Gorbach conceived of a national survey of testing susceptibility of *Bacteroides fragilis* and related species to various antimicrobials. The reasons for the survey were the recognition that plasmid-mediated transferable antibiotic resistance to clindamycin could be shown [1], concern that such transferable resistance might render clindamycin to be ineffective, recognition that susceptibility of *Bacteroides* species to antimicrobials was associated with an improved outcome [2–5], and evidence that different susceptibilities of *Bacteroides* species to antimicrobials depended on geographic location [6]. Finally, because hospital laboratories usually lack the capacity to test *Bacteroides* species for susceptibility, clinicians needed information about regional or national patterns, to choose appropriate agents for empirical therapy.

Approximately 9 health care centers and a number of investigators have been involved in the survey since

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**Table 1. Overview of the Survey on *Bacteroides* Species (1981–2007)**

| Variable | 1981 | 1997–2007 |
|---|---|---|
| No. of health care centers | 9 | 9–10 |
| Method | Tufts Anaerobic Laboratory supplemented brain-heart infusion agar with $1 \times 10^6$ inoculum | CLSI (NCCLS before 1997) supplemented brucella blood agar with $1 \times 10^8$ inoculum |
| Antibiotics tested | Piperacillin, cephalosporins, cephamycins, tetracycline, clindamycin, metronidazole, chloramphenicol | Inhibitor combinations, carbapenems, cefoxitin, tigecycline, clindamycin, fluoroquinolones, metronidazole, chloramphenicol |
| Program used for statistical analysis | TRS/80 Model I (Radio Shack) | SAS for Windows (SAS Institute) |

**NOTE.** The Principal Investigators of the study were Francis P. Tally (1981–1986), George J. Cuchural, Jr. (1986–1990), and David R. Snydman (1986–2007). CLSI, Clinical and Laboratory Standards Institute; NCCLS, National Committee on Clinical Laboratory Standards.

its beginning (Table 1). In the method used from 1981 through 1997, supplemented brain-heart infusion agar was given an inoculum of $1 \times 10^6$ [7]. In 1997, the survey adopted the method recommended that year by the Clinical and Laboratory Standards Institute (CLSI; formerly, National Committee on Clinical Laboratory Standards); with this method, supplemented brucella blood agar used an inoculum of $1 \times 10^8$ [8]. The antibiotics tested are listed in Table 1. Over the last 27 years of the survey, the test antibiotics changed as newer agents were introduced. The agents that were continuously tested were clindamycin, cefoxitin, metronidazole, and chloramphenicol. Statistical analysis was first performed using a TRS/80 Model 1 computer from Radio Shack. There is some irony that contemporary wristwatches probably have more computing power than this early version of the TRS/80. Current analyses are performed using SAS, version 8.01, for Windows (SAS Institute).

In the early 1980s, among isolates of the *Bacteroides* species (which were analyzed as a group), 6% were resistant to clindamycin and 8% were resistant to cefoxitin [9, 10]. In contrast, by 2004, clindamycin resistance had increased to 31.6%, although cefoxitin resistance remained relatively constant at 8% [11]. Table 2 shows the changes in susceptibility that occurred over the 3 decades of the study.

The survey group has been responsible for >15 publications [6, 9–21], and a number of themes and principles have emerged. One is that the susceptibility of *Bacteroides* species to antimicrobials is important to outcome, even in the presence of mixed infections. For instance, in the context of *Bacteroides* bacteremia due to mixed infection, the survey group revealed that outcome and susceptibility are related [5]. The survey group has been instrumental in establishing susceptibility criteria for certain antibiotics for the CLSI. For drug development studies, the survey has provided a framework for activity that provides pharmaceutical companies with data for further clinical development [22]. In addition, the group has made major contributions toward the use of different media and testing methods [23]. For this symposium in honor of Frank Tally, MD, we analyzed the data on drug susceptibility of *Bacteroides* species from 1997 through 2007, to examine trends over time for certain drug and organism combinations, as well as regional variation.

## METHODS

***Medical centers.*** From 1997 through 2007, isolates were referred from the following medical centers representing various regions of the United States: Albany Medical Center, Albany, New York (1997–2003); Carolinas Medical Center, Charlotte, North Carolina (1997, 1998, 2003, and 2004); Danbury Hospital, Danbury, Connecticut (1997); Duke University Medical Center, Durham, North Carolina (1997–2006); Loyola University Medical Center, Maywood, Illinois (1997–2006); New England Medical Center, Boston, Massachusetts (1997–2006); Mount Sinai Medical Center, New York, New York (2000–2006); Pittsburgh Veterans Administration Center, Pittsburgh, Pennsylvania (1997–2005); R. M. Alden Research Laboratories, Santa Monica, California (1997–2006); University of Maryland

**Table 2. Percent Resistance of All Species of the *Bacteroides fragilis* Group to Select Antibiotics from 1981 through 2007**

| | Resistance, % | | |
|---|---|---|---|
| Antibiotic | 1981–1989 ($n$ = 1229) | 1990–1999 ($n$ = 2080) | 2000–2007 ($n$ = 3140) |
| Clindamycin | 5–6 | 23 | 31 to >35 |
| Cefoxitin | 4–8 | ~12 | 9 |
| Imipenem | <1 | <1 | <1 |
| Piperacillin-tazobactam | Not tested | <1 | <1 |
| Trovafloxacin | Not tested | 16 | >40 |
| Metronidazole | None | None | 2 isolates[a] |
| Chloramphenicol | None | None | None |

[a] Not expressed as a percentage because of the small number of isolates.

Medical Center, Baltimore, Maryland (2004–2006); University of Michigan Medical Center, Ann Arbor, Michigan (1997–2006); Wadsworth Veterans Administration Hospital, Los Angeles, California (1997–2002); and Mayo Clinic, Rochester, Minnesota (2007).

***Antimicrobial agents.*** Standard powders of the antibiotics were obtained from the following manufacturers: cefoxitin, ertapenem, and imipenem from Merck; ampicillin and sulbactam from Pfizer; piperacillin, tazobactam, and tigecycline from Wyeth-Ayerst Research; meropenem from AstraZeneca Pharmaceuticals; doripenem (tested only during 2006–2007) from Johnson & Johnson; moxifloxacin from Bayer Pharmaceuticals; and clindamycin, metronidazole, and chloramphenicol from Sigma-Aldrich.

***Bacterial isolates.*** A total of 6544 nonduplicated clinical isolates of the *B. fragilis* group were referred for susceptibility testing to the Special Studies Laboratory at Tufts Medical Center (Boston, MA) by the medical centers participating in the survey. The isolates were shipped on prereduced agar slants and were stored until the time of testing. Identification of the isolates was confirmed using rapid methodology (API 20A [bioMèrieux], RapID Ana II [Remel], or An-IDENT [bioMèrieux]). If results obtained by rapid methods were inconclusive, identification was confirmed by standard methods described in the *Wadsworth Anaerobic Bacteriology Manual* and/or in the *Anaerobic Laboratory Manual* of the Virginia Polytechnic Institute [24–26].

***Susceptibility testing.*** Minimum inhibitory concentrations (MICs) were determined by agar dilution method in accordance with CLSI recommendations [8, 27, 28]. The plates were prepared on the day of the test with use of enriched brucella agar (brucella agar supplemented with 5% lysed defibrinated sheep red blood cells and 1 $\mu$g/mL vitamin K). For the preparation of the inocula, the organisms were grown to logarithmic phase, and the turbidity was adjusted to that of a 0.5 McFarland standard ($\sim 1 \times 10^8$ colony-forming units/mL). The inocula were delivered to the surface of the agar plate with use of a Steers replicator, resulting in an organism concentration of $1 \times 10^5$ colony-forming units/spot. The inoculated plates were incubated at 37°C in an anaerobic chamber for 48 h. *B. fragilis* American Type Culture Collection 25285 and *Bacteroides thetaiotaomicron* American Type Culture Collection 29741 were used as controls in all tests. Tests were repeated when the MICs of the control organisms were outside the range specified by the National Committee on Clinical Laboratory Standards (1997–2004) or CLSI (2005–2007) recommendations [28, 29].

***Data analysis.*** Data were stored in Microsoft Excel spreadsheets. Statistical analysis was performed using SAS for Windows, version 8.01 (SAS Institute). Trends for increased or decreased drug resistance over the 10-year study period were determined using the Cochran-Armitage test [30]. Breakpoints for resistance to the antibiotics were those recommended by the CLSI [29]. Breakpoints established by the US Food and Drug Administration for resistance in anaerobes were used for tigecycline [31]. Trends for increased or decreased MICs over time were evaluated using linear regression analysis on the $\log_{10}$ MIC results.

## RESULTS

Table 3 shows the distribution, by species, of the 6574 isolates included in the study. *B. fragilis* continued to be the most frequently isolated species during the 10 years of our study; however, there was a trend toward a reduction in the frequency of isolation from a mean of 52% during the first 8 years to a mean of 48% during the final 2 years, in conjunction with an increase to 52% in the frequency of isolation of the non–*B. fragilis Bacteroides* species. *B. thetaiotaomicron* was the second most frequently isolated organism (19.3%). Isolates of *B. ovatus* comprised 10.3% of the total isolates, and 6% were *Bacteriodes vulgatus. Bacteroides caccae,* a species previously included among the "other" *Bacteroides* category, was isolated at higher frequency, similar to that of *Bacteriodes distasonis* (3.9%) and *Bacteroides uniformis* (4.4%); thus, it is listed separately during the last 2 years of the study.

Understandably, the majority of blood isolates were *B. fragilis.* The majority of the nonblood isolates were found in samples from patients with intra-abdominal infection.

Table 4 shows a summary of the susceptibilities of 1351 isolates referred from 2005 through 2007. Percent resistance was calculated using breakpoints recommended for the respective antibiotic by the CLSI or Food and Drug Administration [28, 30]. For the carbapenems, low resistance was observed in *B. distasonis* and *B. uniformis.* In this class of agents, ertapenem also showed low resistance in *B. ovatus* and *B. thetaiotaomicron.* The activity of piperacillin-tazobactam was similar to that of the carbapenems and higher than that of ampicillin-sulbactam, which continued to show increased resistance in *B. distasonis.* Cefoxitin activity against *B. distasonis* was higher from 2005 through 2007 (11.1%) than it was from 1997 through 2004 (29.9%; data not shown). Resistance of *B. ovatus* to cefoxitin during this period (~18%) was similar to that during previous years.

Tigecycline was the most active antibiotic among the non–$\beta$-lactam agents (clindamycin, linezolid, tigecycline, moxifloxacin, and trovafloxacin). The highest resistance to tigecycline was observed among the "other" *Bacteroides* species group. The second most active agent among this group was linezolid, with a resistance ranging from 0% for *B. uniformis* to 11.2% for *B. distasonis* and *B. ovatus.* Resistance of *Bacteroides* species to clindamycin ranged from 14.3% for *B. distasonis* to 49.2% for *B. uniformis.*

More than half of the *B. vulgatus* isolates were resistant to

**Table 3. Distribution of the Species in the *Bacteroides fragilis* Group (1997–2007)**

| Species | No. (%) of isolates | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 1997 | 1998 | 1999 | 2000 | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | All |
| *Bacteroides caccae*[a] | … | … | … | … | … | … | … | … | 21 (4.6) | 16 (4.0) | 9 (3.0) | 46 (3.9) |
| *Bacteroides distasonis* | 41 (6.4) | 52 (6.2) | 35 (5.8) | 36 (6.1) | 17 (3.1) | 32 (5.7) | 28 (3.9) | 33 (4.5) | 18 (4.0) | 16 (4.0) | 26 (5.2) | 334 (5.1) |
| *B. fragilis* | 336 (52.5) | 434 (51.5) | 314 (52.2) | 288 (48.9) | 286 (51.7) | 277 (49.6) | 378 (53.2) | 408 (56.0) | 203 (44.8) | 198 (49.4) | 249 (50.1) | 3371 (51.3) |
| *Bacteroides ovatus* | 67 (10.5) | 120 (14.3) | 57 (9.5) | 61 (10.4) | 73 (13.2) | 45 (8.1) | 71 (10.0) | 51 (7.0) | 45 (9.9) | 32 (8.0) | 56 (11.3) | 678 (10.3) |
| *Bacteroides thetaiotaomicron* | 102 (15.9) | 128 (15.2) | 118 (19.6) | 136 (23.1) | 98 (17.7) | 123 (22.0) | 152 (21.4) | 121 (16.6) | 111 (24.5) | 83 (20.7) | 96 (19.3) | 1268 (19.3) |
| *Bacteroides uniformis* | 44 (6.9) | 28 (3.3) | 9 (1.5) | 11 (1.9) | 16 (2.9) | 24 (4.3) | 23 (3.2) | 42 (5.8) | 20 (4.4) | 21 (5.2) | 17 (3.4) | 255 (3.9) |
| *Bacteroides vulgatus* | 32 (5.0) | 45 (5.3) | 45 (7.5) | 35 (5.9) | 40 (7.2) | 31 (5.6) | 29 (4.1) | 49 (6.7) | 27 (6.0) | 27 (6.7) | 33 (6.6) | 393 (6.0) |
| Other[b] | 18 (2.8) | 35 (4.2) | 24 (4.0) | 22 (3.7) | 23 (4.2) | 26 (4.7) | 29 (4.1) | 25 (3.4) | 8 (1.8) | 8 (2.0) | 11 (2.2) | 229 (3.5) |
| All in *B. fragilis* group | 640 (10.4) | 842 (13.7) | 602 (9.8) | 589 (9.6) | 553 (9.0) | 558 (9.1) | 710 (11.6) | 729 (12.4) | 453 (6.9) | 401 (6.1) | 497 (7.6) | 6574 (100) |
| Non–*B. fragilis Bacteroides* species | 304 (47.5) | 408 (48.5) | 288 (47.8) | 301 (51.1) | 267 (48.3) | 281 (50.4) | 332 (46.8) | 321 (44.0) | 250 (55.2) | 203 (50.6) | 248 (49.9) | 3203 (48.7) |

[a] *B. caccae* was listed as a separate species during 2005–2007 only; during 1997–1004, it was included in the "other" category.

[b] During 1997–2004, "other" includes 150 *B. caccae* isolates, 34 *Bacteroides eggerthii* isolates, 2 *Bacteroides merdae* isolates, 15 *Bacteroides stercoris* isolates, and 1 unidentified isolate. During 2005–2007, "other" includes 14 *B. eggerthii* isolates, 4 *B. merdae* isolates, 1 *Bacteroides nordii* isolate, and 8 other *Bacteroides* isolates.

**Table 4. Susceptibilities of 1351 Isolates in the *Bacteroides fragilis* Group (2005–2007)**

| Species (no. [%] of isolates) | Doripenem[a] | Ertapenem | Imipenem | Meropenem | Amp-Sul | Pip-Tzb | Tigecycline | Cefoxitin | Clindamycin | Moxifloxacin | Trovafloxacin | Linezolid |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Bacteroides caccae* (46 [35]) | | | | | | | | | | | | |
| MIC range, mg/mL | 0.25–4 | 0.25–8 | <0.125 to 4 | <0.125 to 4 | 1–16 | 0.5–16 | 0.25–16 | 4–128 | <0.5 to >128 | 0.5–64 | 0.25–16 | 2–8 |
| $MIC_{50}$, mg/mL | 0.5 | 0.5 | 0.25 | 0.25 | 4 | 1 | 2 | 16 | 1 | 4 | 2 | 4 |
| $MIC_{90}$, mg/mL | 0.5 | 2 | 1 | 1 | 16 | 8 | 8 | 32 | >128 | 32 | 8 | 4 |
| Resistance, % | 0 | 0 | 0 | 0 | 0 | 0 | 4.1 | 6.1 | 36.7 | 40.8 | 30.6 | 6.1 |
| *Bacteroides distasonis* (60 [4.5]) | | | | | | | | | | | | |
| MIC range, mg/mL | <0.125 to 2 | 0.25–8 | 0.25–4 | <0.125 to 8 | <0.5 to 64 | <0.25 to 16 | 0.25–32 | 4–32 | <0.5 to >128 | 42.9 | 0.5–16 | 2–8 |
| $MIC_{50}$, mg/mL | 0.5 | 1 | 0.5 | 0.25 | 8 | 8 | 2 | 16 | 1 | 1 | 2 | 4 |
| $MIC_{90}$, mg/mL | 2 | 2 | 2 | 2 | 32 | 16 | 8 | 32 | 128 | 16 | 8 | 8 |
| Resistance, % | 0 | 0 | 0 | 0 | 20.6 | 0 | 3.2 | 11.1 | 14.3 | 42.9 | 38.1 | 11.2 |
| *Bacteroides fragilis* (650 [47.6]) | | | | | | | | | | | | |
| MIC range, mg/mL | <0.125 to 16 | 0.25 to >16 | <0.125 to >16 | 1.1 | <0.5 to 128 | <0.25 to 512 | 0.25–32 | 2–128 | <0.5 to >128 | 0.125–64 | 0.5–32 | 1–8 |
| $MIC_{50}$, mg/mL | 0.5 | 0.5 | 0.25 | 0.25 | 4 | 0.5 | 1 | 16 | 1 | 1 | 1 | 4 |
| $MIC_{90}$, mg/mL | 2 | 2 | 0.5 | 1 | 16 | 2 | 8 | 32 | 128 | 16 | 8 | 4 |
| Resistance, % | 1.3 | 1.4 | 0.3 | 1.2 | 2.8 | 0.6 | 4.7 | 4.1 | 23.9 | 32.1 | 27.9 | 5.6 |
| *Bacteroides ovatus* (133 [9.5]) | | | | | | | | | | | | |
| MIC range, mg/mL | 0.25–8 | 0.25–16 | <0.125 to 8 | <0.125 to 8 | 1–64 | 0.5–32 | 0.25–16 | 8–128 | <0.5 to >128 | 0.5–128 | 0.5–16 | 1–8 |
| $MIC_{50}$, mg/mL | 0.5 | 1 | 0.25 | 0.25 | 4 | 4 | 1 | 32 | 2 | 4 | 2 | 4 |
| $MIC_{90}$, mg/mL | 1 | 4 | 1 | 1 | 16 | 8 | 8 | 64 | >128 | 32 | 8 | 8 |
| Resistance, % | 0 | 2.2 | 0 | 0 | 4.5 | 0 | 5.2 | 17.9 | 45.5 | 38.8 | 16.4 | 11.2 |
| *Bacteroides thetaiotaomicron* (290 [22.0]) | | | | | | | | | | | | |
| MIC range, mg/mL | <0.125 to 8 | <0.125 to 16 | <0.125 to 8 | <0.125 to 8 | 1–64 | 0.5 to >128 | 0.125–32 | 4 to >128 | <0.5 to >128 | 0.25–64 | 0.25–128 | 1–16 |
| $MIC_{50}$, mg/mL | 0.5 | 1 | 0.25 | 0.25 | 4 | 8 | 1 | 32 | 4 | 2 | 1 | 4 |
| $MIC_{90}$, mg/mL | 1 | 4 | 1 | 1 | 16 | 16 | 8 | 32 | >128 | 32 | 8 | 8 |
| Resistance, % | 0 | 1.3 | 0 | 0 | 4.9 | 0.6 | 5.8 | 6.8 | 39.8 | 33.0 | 21.3 | 10.0 |
| *Bacteroides uniformis* (58 [4.2]) | | | | | | | | | | | | |
| MIC range, mg/mL | <0.125 to 2 | <0.125 to 32 | 0.25–16 | <0.125 to 32 | 1–32 | 0.5–16 | 0.125–16 | 2–64 | <0.5 to >128 | 0.5–128 | 1–16 | 1–4 |
| $MIC_{50}$, mg/mL | 0.5 | 0.5 | 0.25 | 0.25 | 4 | 2 | 1 | 16 | 4 | 8 | 2 | 2 |
| $MIC_{90}$, mg/mL | 1 | 2 | 1 | 1 | 16 | 8 | 8 | 32 | >128 | 32 | 8 | 4 |
| Resistance, % | 0 | 1.7 | 1.7 | 1.7 | 1.7 | 0 | 6.8 | 10.2 | 49.2 | 40.7 | 33.9 | 0 |
| *Bacteroides vulgatus* (87 [6.7]) | | | | | | | | | | | | |
| MIC range, mg/mL | <0.125 to 2 | <0.125 to 4 | <0.125 to 8 | <0.125 to 4 | 1–32 | 0.5 to >128 | 0.25–8 | 2–64 | <0.5 to >128 | 0.25– 128 | 0.25–64 | 1–8 |
| $MIC_{50}$, mg/mL | 0.5 | 0.5 | 0.5 | 0.5 | 4 | 4 | 1 | 8 | 1 | 16 | 4 | 2 |
| $MIC_{90}$, mg/mL | 2 | 2 | 2 | 2 | 16 | 16 | 4 | 32 | >128 | 64 | 16 | 4 |
| Resistance, % | 0 | 0 | 0 | 0 | 4.3 | 1.1 | 0 | 7.4 | 42.6 | 56.4 | 54.3 | 7.4 |

**NOTE.** Twenty-seven other *Bacteroides* species are not included in the table: 14 *Bacteroides eggerthii* isolates, 4 *Bacteroides merdae* isolates, 1 *Bacteroides nordii* isolate, and 8 "other" *Bacteroides* isolates. Breakpoints for resistance, as recommended by the Clinical and Laboratory Standards Institute were ⩾16 mg/mL for ertapenem, imipenem, and meropenem; ⩾128 mg/mL for piperacillin-tazobactam (Pip-Tzb); ⩾32 mg/mL for ampicillin-sulbactam (Amp-Sul); ⩾64 mg/mL for cefoxitin; and ⩾8 mg/mL for clindamycin, moxifloxacin, and trovafloxacin. The breakpoint for resistance for doripenem was the same as that recommended for other carbapenems (⩾16 mg/mL), and the breakpoint for resistance for tigecycline was ⩾16 mg/mL, as recommended by the US Food and Drug Administration. MIC, minimum inhibitory concentration; $MIC_{50}$, MIC required to inhibit the growth of 50% of organisms; $MIC_{90}$, MIC required to inhibit the growth of 90% of organisms.

[a] Doripenem data are for isolates from 2006 and 2007 only.

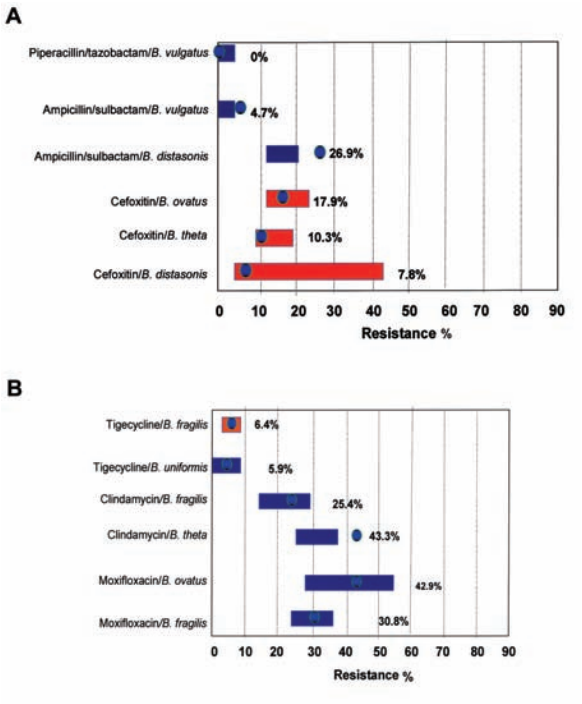


**Figure 1.** *A,* Resistance of *Bacteroides* species to selected antibiotics over time (1997–2007). Blue bars indicate an increase in resistance during 1997–2006, blue circles indicate resistance during 2007, and red bars indicate instances in which resistance was lower in 2006 than in 2007. *B,* Resistance of *Bacteroides* species to tigecycline, clindamycin, and moxifloxacin (2000–2007). Blue bars indicate an increase in resistance during 2000–2006, blue circles indicate resistance during 2007, and red bars indicate instances in which resistance was lower in 2000 than in 2006.

moxifloxacin (56.4%) and trovafloxacin (54.3%). Resistance to these 2 fluoroquinolones increased with time for most of the species.

Isolates in the "other" *Bacteroides* species group *(Bacteroides eggerthii, Bacteroides merdae,* and *Bacteroides nordii)* showed a relatively high rate of resistance to tigecycline. In this group, we also observed higher rates of resistance to moxifloxacin (29.6%) and to clindamycin (25.9%).

In general, the MICs required to inhibit the growth of 90% of organisms ($MIC_{90}$) for the carbapenems, piperacillin-tazobactam, and tigecycline against all the species in the group were below the breakpoints for resistance. By comparison, the $MIC_{90}$ of clindamycin, moxifloxacin, and trovafloxacin were equal to or greater than the breakpoint for resistance against all species. In addition, the MIC required to inhibit the growth of 50% of organisms for both fluoroquinolones against *B. vulgatus* was equal to the resistance breakpoint of 8 $\mu$g/mL. The $MIC_{90}$ of ampicillin-sulbactam and cefoxitin was equal to the resistance breakpoint against *B. distasonis* and *B. ovatus,* respectively.

Figure 1*A* and 1*B* show the rates of resistance over time (1997–2007) for selected antibiotic-species combinations. Figure 1*A* shows the variation in resistance for both inhibitor combinations to *B. vulgatus.* The data on *B. vulgatus* for the last year (2007) indicate that there was no resistance to piperacillin-tazobactam, whereas resistance to ampicillin-sulbactam remained approximately the same during 2006 and 2007 (4.7% and 2.9%, respectively). There was an increase in resistance to ampicillin-sulbactam in *B. distasonis* of ~25% over the 11-year study period. Of interest, resistance to cefoxitin in *B. ovatus, B. thetaiotaomicron,* and *B. distasonis* was considerably reduced during the study period. This trend is particularly notable for *B. distasonis,* in which resistance was reduced by >30%.

Figure 1*B* shows resistance rates to tigecycline, clindamycin, and moxifloxacin from 2000 through 2007. Resistance to tigecycline in *B. fragilis* and *B. uniformis* remained stable, although during 2007, the rate was somewhat higher for *B. fragilis* (6.4%) and lower for *B. uniformis* (5.9%) than during the previous year. Resistance to clindamycin increased by ~15% for *B. fragilis* and *B. thetaiotaomicron* (29% and 36.3%, respectively, during 2006). Resistance to moxifloxacin was quite high; it increased to 42.9% for *B. ovatus* during 2007 and to ~30% for *B. fragilis.*

From 2002 through 2007, 3 metronidazole-resistant isolates were confirmed in our survey; the first of these was isolated in 2002 [11]. Resistance to metronidazole has been increasingly reported in Europe but not in the United States.

Throughout the survey, specifically from 2003 through 2007, susceptibility to select antibiotics varied by health care center and species. For some antibiotics, such as clindamycin or moxifloxacin, the range of resistance varied greatly by health care center. Analysis of year-to-year variation among health care

**Figure 2.** Tufts New England Medical Center Infectious Diseases Division, June 1979. Bottom row (left to right): Francis P. Tally, Jeffrey A. Gelfand, Sherwood L. Gorbach, Michael Barza, Te-Wen Chang, John G. Bartlett. Middle row (left to right): Ted Butler, David R. Snydman, Katherine McGowan, Gary Simon, Michael Lauerman. Top row (left to right): Stephen Kornfeld, Cesar Elster, Ray Saginur, Keith Joiner.

centers revealed some differences, but most resistance rates remained relatively constant (data not shown).

## CONCLUSIONS

The survey provided several insights with respect to susceptibility of *Bacteroides* species to drugs. Some drugs had constant or increased activity, whereas others had decreased activity against the species. The trends were not always predictable, varying by region and institution. However, some important species–drug susceptibility patterns were found: *B. ovatus* was more resistant to the carbapenems than were other *Bacteroides* species, *B. vulgatus* was more resistant to piperacillin-tazobactam, *B. distasonis* was more resistant to ampicillin-sulbactam and cefoxitin, *B. ovatus* and *B. uniformis* were highly resistant to moxifloxacin, and moxifloxacin resistance rates among *B. vulgatus* were >50%. "Other" *Bacteroides* species were more resistant to tigecycline. In general, *B. fragilis* is more susceptible to antimicrobials than are other *Bacteroides* species. These data provide a general guide for the clinician in treating anaerobic infections.

The survey should widen its scope in the future. It would be interesting to cover the molecular relatedness of strains. The relationship between antimicrobial use and resistance to these agents would be another important focus. Are fecal isolates more susceptible than clinical isolates? Molecular detection of metronidazole and carbapenem resistance, as well as other genetic markers, is another area of increasing importance. Finally, Internet-based real-time reporting of drug resistance is becoming more widespread and could be applied to the survey.

The anaerobic susceptibility survey has been ongoing for 29 years, thanks in part to the vision of Francis P. Tally (Figure 2). It has evolved and generated an enormous amount of clinically useful microbiological data for the practicing clinician.


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