

Controlled Clinical Comparison of BACTEC Plus Anaerobic/F to Standard Anaerobic/F as the Anaerobic Companion Bottle to Plus Aerobic/F Medium for Culturing Blood from Adults

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To determine the optimal anaerobic companion bottle to pair with BACTEC Plus Aerobic/F medium for recovery of pathogenic microorganisms from adult patients with bacteremia and fungemia, we compared Plus Anaerobic/F bottles with Standard Anaerobic/F bottles, each of which was filled with 4 to 6 ml of blood. The two bottles were paired with a Plus Aerobic/F bottle filled with 8 to 12 ml of blood. A total of 14,011 blood culture sets were obtained. Of these, 11,583 sets were received with all three bottles filled adequately and 12,257 were received with both anaerobic bottles filled adequately. Of 818 clinically important isolates detected in one or both adequately filled anaerobic bottles, significantly more staphylococci ($P < 0.001$), streptococci ($P < 0.005$), *Escherichia coli* isolates ($P < 0.02$), *Klebsiella pneumoniae* isolates ($P < 0.005$), and all microorganisms combined ($P < 0.001$) were detected in Plus Anaerobic/F bottles. In contrast, significantly more anaerobic gram-negative bacilli were detected in Standard Anaerobic/F bottles ($P < 0.05$). Of 397 unimicrobial episodes of septicemia, 354 were detected with both pairs, 30 were detected with Plus Aerobic/F–Plus Anaerobic/F pairs only, and 13 were detected with Plus Aerobic/F–Standard Anaerobic/F pairs only ($P < 0.05$). Significantly more episodes of bacteremia caused by members of the family *Enterobacteriaceae* ($P < 0.05$) and aerobic and facultative gram-positive bacteria ($P < 0.025$) were detected with Plus Anaerobic/F bottles only. In a paired-bottle analysis, 810 of 950 isolates were recovered from both pairs, 90 were recovered from Plus Aerobic/F–Plus Anaerobic/F pairs only, and 50 were recovered from Plus Aerobic/F–Standard Anaerobic/F pairs only ($P < 0.001$). Paired Plus Aerobic/F–Plus Anaerobic/F bottles yielded significantly more staphylococci ($P < 0.001$), streptococci ($P < 0.05$), and members of the family *Enterobacteriaceae* ($P < 0.001$). We conclude that Plus Anaerobic/F bottles detect more microorganisms and episodes of bacteremia and fungemia than Standard Anaerobic/F bottles as companion bottles to Plus Aerobic/F bottles in the BACTEC 9240 blood culture system.

During the past decade, several investigators have noted a declining incidence of bacteremia caused by anaerobic organisms (4, 16, 27; J. W. Gray and S. J. Pedler, Letter, *Am. J. Med.* **93**:706–707, 1992). During the same period there has been a reported increase in the proportion of blood cultures that yield pathogenic fungi (16, 27). Because of these observations, some investigators have questioned the practice of routinely inoculating half of the collected blood volume into anaerobic blood culture bottles, suggesting that overall yield may be increased by culturing all of the blood in aerobic bottles, restricting use of anaerobic blood cultures to patients in whom anaerobic bacteremia is likely to occur (5, 7, 14, 16, 19, 23, 30). Other investigators have suggested that anaerobic blood cultures are no longer as helpful clinically because bacteremia caused by anaerobic organisms occurs in predictable clinical scenarios, the results do not affect patient care, or empiric therapy often is not changed on the basis of the results of blood cultures (7,

11, 19, 23). Published data do, however, indicate that the incidence of bacteremia caused by anaerobic organisms has not decreased (or has even increased) in some patient populations, that bacteremia caused by anaerobic organisms can occur in a clinically unpredictable manner, and that anaerobic blood culture results affect therapeutic decisions (3, 6, 17, 21; W. R. Gransden, S. J. Eykyn, and I. Phillips, Letter, *Rev. Infect. Dis.* **13**:1255–1256, 1991; Gray and Pedler, Letter; T. V. Riley and M. A. Aravena, Letter, *Eur. J. Clin. Microbiol. Infect. Dis.* **14**:73–75, 1995). Therefore, some investigators continue to advocate routine use of anaerobic blood culture bottles (3, 6; Gray and Pedler, Letter). The decision as to which approach to take will depend, in part, upon the results of controlled clinical trials that compare the relative yields of aerobic and anaerobic blood culture bottles. For such trials to be meaningful, it will be necessary to compare the best aerobic and anaerobic bottles. To determine which anaerobic formulation is best, controlled clinical trials are needed that compare the different anaerobic formulations available with each blood culture system.

The BACTEC 9240 system (Becton Dickinson BioSciences, Sparks, Md.) is a continuous monitoring blood culture system that uses several medium formulations. Although the aerobic formulations have been studied extensively, the anaerobic for-

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TABLE 1. Comparative yields of clinically important bacteria and fungi from BACTEC Plus Anaerobic/F and Standard Anaerobic/F blood culture bottles

Microorganism	No. of isolates recovered from:			P
	Both bottles	Plus Anaerobic/F bottles only	Standard Anaerobic/F bottles only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	139	120	9	<0.001
Coagulase-negative staphylococci	61	54	10	<0.001
Enterococci ^b	51	16	14	NS ^a
Streptococci ^c	28	11	0	<0.005
Other gram-positive bacteria ^d	2	0	3	NS
Gram-negative bacilli				
<i>Escherichia coli</i>	47	22	8	<0.02
<i>Klebsiella pneumoniae</i>	48	20	4	<0.005
Other <i>Enterobacteriaceae</i> ^e	50	9	5	NS
Nonfermenters ^f	13	9	4	NS
Anaerobic bacteria				
Gram-positive ^g	6	5	4	NS
Gram-negative ^h	10	4	14	<0.05
Yeasts ⁱ	6	8	4	NS
All microorganisms	461	278	79	<0.001

^a NS, nonsignificant ($P > 0.050$).

^b Includes 53 *Enterococcus faecalis*, 21 *Enterococcus faecium*, and 6 *Enterococcus durans* isolates and 1 *Enterococcus* sp.

^c Includes 15 viridans group streptococci, 9 *Streptococcus pneumoniae* isolates, 8 group B streptococci, 4 group G streptococci, 2 nutritionally deficient streptococci, and 1 group A streptococcus.

^d Includes two *Listeria monocytogenes* isolates, one *Aerococcus viridans* isolate, and one *Lactobacillus* sp.

^e Includes 23 *Serratia marcescens*, 14 *Enterobacter cloacae*, 8 *Klebsiella oxytoca*, 6 *Enterobacter aerogenes*, 5 *Proteus mirabilis*, 3 *Proteus vulgaris*, and 3 *Citrobacter diversus* isolates, 1 *Morganella morganii* isolate, and 1 *Salmonella* sp.

^f Includes 16 *Pseudomonas aeruginosa*, 4 *Pseudomonas fluorescens*, 2 *Achromobacter xylosoxidans* subsp. *xylosoxidans*, and 2 *Stenotrophomonas maltophilia* isolates, 1 *Acinetobacter baumannii* isolate, and 1 *Acinetobacter* sp.

^g Includes six *Clostridium septicum*, three *Clostridium tertium*, two *Clostridium innocuum*, and two *Clostridium* spp. isolates and one isolate each of *Clostridium perfringens* and *Clostridium ramosum*.

^h Includes 11 *Bacteroides fragilis*, 5 *Bacteroides thetaiotaomicron*, 2 *Bacteroides oris-Bacteroides buccae*, 2 *Bacteroides* spp., 2 *Fusobacterium nucleatum*, and 2 *Porphyromonas loeschei* isolates, 1 isolate each of *Bacteroides fragilis* group, *Bacteroides intermedius*, and *Bacteroides uniformis*, and 1 *Fusobacterium* sp.

ⁱ Includes eight *Candida glabrata*, seven *Candida tropicalis*, and three *Candida albicans* isolates.

mulations have not been evaluated to the same degree in controlled clinical trials. In the study described here, we compared the BACTEC Plus Anaerobic/F bottle with the Standard Anaerobic/F bottle for recovery of bacteria and fungi from adult patients. The two anaerobic bottles were paired with the Plus Aerobic/F bottle, as that bottle has previously been shown to recover pathogenic microorganisms with yields superior to those from non-resin-containing bottles (2, 10, 24) and equivalent to those from other high-volume resin-containing bottles (9, 18, 22).

MATERIALS AND METHODS

Blood culture and collection. Blood samples for culture were collected from adult patients hospitalized at Duke University Medical Center (DUMC), Robert Wood Johnson University Hospital (RWJUH), and Denver Health Medical Center (DHMC). Institutional review board approval was obtained prior to the study at each of the study sites. All blood cultures were performed per physician order as part of routine patient care. Venipuncture sites were disinfected with povidone iodine and allowed to dry. The povidone iodine was removed with isopropyl alcohol as a second disinfecting step. Up to 20 ml of blood was drawn from veins with a sterile needle and syringe. Needles were not changed prior to inoculation of blood culture bottles.

Adequacy of blood volume. Upon receipt in the laboratories, the volume of blood inoculated into each bottle was assessed visually by comparison with known volume standards. Plus Aerobic/F bottles were categorized by the volume of fill as underfilled (<8 ml), adequately filled (8 to 12 ml), or overfilled (>12

ml). Plus Anaerobic/F bottles were similarly categorized by the volume of fill as underfilled (<4 ml), adequately filled (4 to 6 ml), or overfilled (>6 ml). All bottles were processed for patient care purposes, irrespective of the volume of blood contained within them.

Bottle processing. All bottles were placed in the instrument (BACTEC 9240) and tested for 5 days according to the manufacturer's recommendations. Bottles flagged by an instrument as positive were removed from the instrument. An aliquot of the blood-broth mixture was removed from the bottle with a sterile needle and syringe. A portion was used for a Gram stain, and the remainder was subcultured onto solid plate media according to the results of the Gram stain. Subsequent isolation and identification of the microbes and antimicrobial susceptibility testing were performed by standard techniques (15).

Clinical assessment. All isolates recovered were reviewed by an infectious diseases physician or a pathologist and were categorized as clinically important, indeterminate as the cause of sepsis, or a contaminant. The assessments were made in accord with published criteria (27). An episode of bacteremia or fungemia was defined as a period that began with the first positive blood culture and that ended when 7 days (2 days for coagulase-negative staphylococci) had passed without another blood sample positive by culture for the same microorganism, regardless of whether samples negative by culture were drawn in the intervening days. When a second clinically important isolate was detected within 3 days of detection of the first isolate, the episode was categorized as polymicrobial.

Data analysis. Data were forwarded to one study site (DUMC), where they were entered into a database (Paradox; Corel, Farmingdale, N.Y.). Comparison of recovery rates was made by the chi-square test with Yates' correction when the number of samples was less than 20 (13). Comparison of the mean speeds of detection of microbial growth was made by the two-tailed *t* test. A cutoff of 72 h was used in these comparisons because (i) most, if not all, pathogenic microorganisms are recovered within this time frame, (ii) most microorganisms recov-

TABLE 2. Mean times to detection of microbial growth for clinically important microorganisms recovered within the first 72 h of incubation in Plus Anaerobic/F and Standard Anaerobic/F blood culture bottles

Microorganism	Avg (range) time (h) to detection ^a		No. of bottles	P
	Plus Anaerobic/F bottles	Standard Anaerobic/F bottles		
Gram-positive cocci				
<i>Staphylococcus aureus</i>	14.6 (6.0–40.3)	17.6 (6.9–47.8)	131	<0.001
Coagulase-negative staphylococci	18.6 (5.7–44.2)	22.9 (6.2–65.0)	59	<0.001
Enterococci	15.0 (3.5–68.0)	14.5 (3.5–45.8)	51	NS ^b
Streptococci	11.3 (4.5–25.0)	12.3 (4.7–32.5)	28	NS
Gram-positive bacilli	27.3 (16.5–38.2)	25.3 (13.0–37.6)	2	NS
Gram-negative bacilli				
Enterobacteriaceae	10.3 (2.0–37.5)	11.5 (2.0–66.1)	142	NS
Nonfermenters	11.2 (2.0–30.1)	12.7 (2.0–27.6)	13	NS
Anaerobic bacteria				
Gram-positive	18.7 (9.1–41.2)	24.2 (9.1–52.8)	6	NS
Gram-negative bacilli	39.5 (24.5–65.9)	27.2 (18.6–55.7)	8	<0.04
Fungi	22.4 (14.2–43.4)	27.8 (14.0–47.7)	5	NS
All microorganisms	14.1 (2.0–68.0)	15.9 (2.0–66.1)	445	<0.001

^a A cutoff of 72 h was used to eliminate bias from cultures that became positive late in the incubation and testing cycle (i.e., outliers).

^b NS, not significant ($P > 0.05$).

ered thereafter are contaminants, and (iii) data from outliers (i.e., pathogenic microorganisms with delayed growth) would likely skew the means.

RESULTS

A total of 12,257 blood culture sets were received with both anaerobic bottles filled adequately (8,966 collected at DUMC, 2,344 collected at RWJUH, and 947 collected at DHMC), yielding 818 clinically important isolates. As shown in Table 1, 461 were recovered from both anaerobic bottles, 278 were recovered from Plus Anaerobic/F bottles only, and 79 were

recovered from Standard Anaerobic/F bottles only ($P < 0.001$). Significantly more *Staphylococcus aureus* isolates ($P < 0.001$), coagulase-negative staphylococci ($P < 0.001$), streptococci ($P < 0.005$), *Escherichia coli* isolates ($P < 0.02$), and *Klebsiella pneumoniae* isolates ($P < 0.005$) were recovered from Plus Anaerobic/F bottles only. In contrast, significantly more gram-negative anaerobic bacteria were recovered from Standard Anaerobic/F bottles only ($P < 0.05$).

As shown in Table 2, the mean times to detection of microbial growth for clinically important microorganisms was

TABLE 3. Comparative detection of episodes of bacteremia and fungemia in Plus Anaerobic/F and Standard Anaerobic/F blood culture bottles

Episode	No. of episodes detected by ^a :			P
	Both sets	Plus sets only	Standard sets only	
Aerobic and facultative microorganisms				
Gram-positive microorganisms ^b	206	17	6	<0.025
Enterobacteriaceae ^d	86	10	2	<0.05
Other gram-negative bacilli ^c	32	0	0	NS ^c
Anaerobic bacteria ^f	6	3	3	NS
Yeasts ^g	24	0	2	NS
All episodes	354	30	13	<0.05

^a Plus sets consisted of a Plus Aerobic/F and Plus Anaerobic/F bottles; Standard sets consisted of Plus Aerobic/F and Standard Anaerobic/F bottles.

^b Includes 117 *Staphylococcus aureus* isolates, 53 coagulase-negative staphylococci, 21 *Enterococcus faecalis* isolates, 10 *Enterococcus faecium* isolates, 7 *Streptococcus pneumoniae* isolates, 6 viridans group streptococci, 3 group B streptococci, 2 group G streptococci, 2 *Listeria monocytogenes* isolates, 2 *Bacillus* spp., 1 *Bacillus cereus* isolate, 1 *Lactobacillus* sp., 1 *Corynebacterium jeikeium* isolate, 1 *Enterococcus* sp., 1 group A streptococcus, and 1 *Aerococcus viridans* isolate.

^c NS, not significant ($P > 0.050$).

^d Includes 37 *Escherichia coli*, 32 *Klebsiella pneumoniae*, 8 *Serratia marcescens*, 7 *Enterobacter cloacae*, 5 *Enterobacter aerogenes*, and 4 *Klebsiella oxytoca* isolates and 1 isolate each of *Citrobacter diversus*, *Citrobacter freundii*, *Morganella morgani*, *Pantoea agglomerans*, and *Proteus mirabilis*.

^e Includes 16 *Pseudomonas aeruginosa*, 5 *Acinetobacter baumannii*, 5 *Stenotrophomonas maltophilia*, and 2 *Burkholderia cepacia* isolates and 1 isolate each of *Acinetobacter lwoffii*, *Achromobacter xylosoxidans* subsp. *xylosoxidans*, *Burkholderia gladioli*, and *Haemophilus influenzae*.

^f Includes six *Bacteroides fragilis* isolates, two *Bacteroides thetaiotaomicron* isolates, one *Fusobacterium* sp., one *Bacteroides* sp., one *Clostridium septicum* isolate, and one *Clostridium* sp.

^g Includes 13 *Candida albicans*, 6 *Candida glabrata*, 2 *Cryptococcus neoformans*, 2 *Candida tropicalis*, and 2 *Candida parapsilosis* isolates and 1 *Histoplasma capsulatum* isolate.

TABLE 4. Comparative yields of microorganisms from Plus Anaerobic/F versus Standard Anaerobic/F bottles paired with Plus Aerobic/F bottles

Episode	No. of isolates detected by ^a :			P
	Both sets	Plus sets only	Standard set only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	233	28	7	<0.001
Coagulase-negative staphylococci	113	15	8	NS ^b
Enterococci ^c	70	10	8	NS
Streptococci ^d	39	6	0	<0.05
Other gram-positive bacteria ^e	10	0	2	NS
Gram-negative bacteria				
<i>Enterobacteriaceae</i> ^f	196	21	7	<0.001
Other gram-negative bacteria ^g	70	0	0	NS
Anaerobic bacteria				
Gram-positive ^h	7	4	3	NS
Gram-negative ⁱ	10	4	13	NS
Yeasts ^j	62	2	2	NS
All microorganisms	810	90	50	<0.001

^a Plus sets consisted of a Plus Aerobic/F and Plus Anaerobic/F bottles; Standard sets consisted of Plus Aerobic/F and Standard Anaerobic/F bottles.

^b NS, Not significant ($P > 0.05$).

^c Includes 51 *Enterococcus faecalis*, 29 *Enterococcus faecium*, and 7 *Enterococcus durans* isolates and 1 *Enterococcus* sp.

^d Includes 16 viridans group streptococci, 12 *Streptococcus pneumoniae* isolates, 9 group B streptococci, 4 group G streptococci, 2 group A streptococci, and 2 nutritionally variant streptococci.

^e Includes four *Listeria monocytogenes* isolates, two *Aerococcus viridans* isolates, two *Bacillus* spp., one *Bacillus cereus* isolate, one *Corynebacterium jeikeium* isolate, one *Lactobacillus* sp., and one diphtheroid.

^f Includes 79 *Escherichia coli*, 78 *Klebsiella pneumoniae*, 22 *Serratia marcescens*, 15 *Enterobacter cloacae*, 8 *Klebsiella oxytoca*, 7 *Enterobacter aerogenes*, 4 *Proteus mirabilis*, 3 *Proteus vulgaris*, and 3 *Citrobacter diversus* isolates, 1 *Citrobacter freundii* isolate, 1 *Enterobacter* sp., 1 *Morganella morgani* isolate, 1 *Pantoea agglomerans* isolate, and 1 *Salmonella* sp.

^g Includes 35 *Pseudomonas aeruginosa*, 11 *Acinetobacter baumannii*, 6 *Stenotrophomonas maltophilia*, 5 *Achromobacter xylosoxidans* subsp. *xylosoxidans*, 4 *Pseudomonas fluorescens*, 2 *Acinetobacter* spp., and 2 *Burkholderia cepacia* isolates, 1 *Burkholderia gladioli* isolate, 1 *Moraxella* sp., 1 *Pseudomonas* sp., 1 *Haemophilus influenzae* isolate, and 1 *Acinetobacter lwoffii* isolate.

^h Includes six *Clostridium septicum* isolates, two *Clostridium tertium* isolates, two *Clostridium* spp., two *Clostridium innocuum* isolates, one *Clostridium perfringens* isolate, and one *Clostridium ramosum* isolate.

ⁱ Includes 11 *Bacteroides fragilis*, 5 *Bacteroides thetaiotaomicron*, 2 *Bacteroides oris-Bacteroides buccae*, 2 *Porphyromonas loeschei*, and 2 *Fusobacterium nucleatum* isolates, 2 *Bacteroides* spp., 1 *Bacteroides fragilis* group isolate, 1 *Bacteroides uniformis* isolate, and 1 *Fusobacterium* sp.

^j Includes 27 *Candida albicans*, 16 *Candida tropicalis*, 11 *Candida glabrata*, 6 *Candida parapsilosis*, 3 *Candida kefyr*, and 2 *Cryptococcus neoformans* isolates and 1 *Histoplasma capsulatum* isolate.

shorter for *Staphylococcus aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.001$), anaerobic gram-negative bacilli ($P < 0.04$), and all microorganisms combined ($P < 0.001$) with Plus Anaerobic/F bottles.

A comparison of detection of septic episodes is shown in Table 3. Of 397 unimicrobial episodes of bacteria and fungemia, 354 were detected with both systems, 30 were detected with Plus Anaerobic/F bottles only, and 13 were detected with Standard Anaerobic/F bottles only ($P < 0.05$). Significantly more septic episodes caused by members of the family *Enter-*

obacteriaceae ($P < 0.05$) and aerobic and facultative gram-positive bacteria ($P < 0.025$) were detected with Plus Anaerobic/F bottles only.

Of the 12,257 sets, 11,583 sets were received with all three bottles filled adequately (8,469 collected at DUMC, 2,218 collected at RWJUH, and 896 collected at DHMC), yielding 950 clinically important isolates. In a comparison of the recovery of clinically important microorganisms in these paired bottle sets (i.e., Plus Aerobic/F bottles paired with either Plus Anaerobic/F or Standard Anaerobic/F bottles) (Table 4), significantly more *Staphylococcus aureus* isolates ($P < 0.001$), streptococci ($P < 0.05$), members of the family *Enterobacteriaceae* ($P < 0.001$), and all microorganisms combined ($P < 0.001$) were recovered from paired Plus Aerobic/F-Plus Anaerobic/F bottles.

For patients receiving appropriate antimicrobial therapy at the time of blood culture (Table 5), significantly more *Staphylococcus aureus* isolates ($P < 0.001$), coagulase-negative staphylococci ($P < 0.02$), members of the family *Enterobacteriaceae* ($P < 0.05$), and all microorganisms combined ($P < 0.001$) were recovered from Plus Anaerobic/F bottles only. In contrast, there were no significant differences in microbial recovery for patients not receiving antimicrobial therapy at the time of blood culture (data not shown).

Significantly more contaminants were recovered from Plus Anaerobic/F bottles than from Standard Anaerobic/F bottles ($P < 0.001$) (Table 6). For specific contaminant microorganisms, significantly more coagulase-negative staphylococci ($P < 0.001$) were recovered from Plus Anaerobic/F bottles, whereas significantly more enterococci ($P < 0.05$) and *Propionibacterium* spp. ($P < 0.001$) were recovered from Standard Anaerobic/F bottles. There were no significant differences in false-positive instrument signals between the two anaerobic bottles.

DISCUSSION

The debate as to the diagnostic yield and cost-effectiveness of anaerobic blood culture bottles continues. The purpose (and design) of this study was not to resolve that issue, which can be resolved only by controlled clinical trials comparing the yields of the best aerobic bottle against the best anaerobic bottle available with a specific blood culture system. Rather, the purpose of this study was to compare the yield and speed of detection of microbial growth of two anaerobic blood culture bottles available for use with the BACTEC 9000 series blood culture instruments.

In the present study, significantly more pathogenic microorganisms were recovered from Plus Anaerobic/F bottles than from Standard Anaerobic/F bottles. Recovery of not only all microorganisms combined but also several groups of bacteria was higher with Plus Anaerobic/F bottles. Plus Anaerobic/F bottles also had a superior ability to detect septic episodes and had an enhanced recovery of pathogenic microorganisms from patients receiving antimicrobial therapy at the time that blood was drawn for culture. Last, when the yields from either of the two anaerobic bottles paired with Plus Aerobic/F bottles were analyzed, the combination of Plus Aerobic/F and Plus Anaerobic/F bottles showed better recovery than the combination of Plus Aerobic/F and Standard Anaerobic/F bottles.

Only gram-negative anaerobic bacteria were recovered more

TABLE 5. Comparative yields of microorganisms in Plus Anaerobic/F versus Standard Anaerobic/F bottles paired with Plus Aerobic/F bottles from patients on therapy

Episode	No. of episodes detected by ^a :			P
	Both sets	Plus sets only	Standard sets only	
Gram-positive bacteria				
<i>Staphylococcus aureus</i>	21	23	1	<0.001
Coagulase-negative staphylococci	12	8	0	<0.02
Other gram-positive bacteria ^b	11	7	4	NS ^c
Gram-negative bacteria				
Enterobacteriaceae ^d	5	8	1	<0.05
Other gram-negative bacilli ^e	1	0	0	NS
Anaerobic bacteria ^f	2	5	5	NS
Yeasts ^g	11	1	0	NS
All microorganisms	63	52	11	<0.001

^a Plus sets consisted of a Plus Aerobic/F and Plus Anaerobic/F bottles; Standard sets consisted of Plus Aerobic/F and Standard Anaerobic/F bottles.

^b Includes 10 *Enterococcus faecalis* isolates, 4 group B streptococci, 2 *Enterococcus faecium* isolates, 2 *Enterococcus durans* isolates, 1 viridans group streptococcus, 1 group A streptococcus, and 1 *Bacillus* sp.

^c NS, not significant ($P > 0.050$).

^d Includes four *Escherichia coli*, four *Klebsiella pneumoniae*, and three *Serratia marcescens* isolates and one isolate each of *Citrobacter diversus*, *Enterobacter aerogenes*, and *Proteus mirabilis*.

^e Includes one *Pseudomonas aeruginosa* isolate.

^f Includes four *Clostridium septicum* isolates, four *Bacteroides thetaiotaomicron* isolates, one *Bacteroides fragilis* isolate, one *Bacteroides fragilis* group isolate, one *Bacteroides* sp., and one *Fusobacterium* sp.

^g Includes four *Candida parapsilosis*, three *Candida tropicalis*, two *Candida albicans*, and two *Candida glabrata* isolates and one *Histoplasma capsulatum* isolate.

often from Standard Anaerobic/F bottles than from Plus Anaerobic/F bottles. The reason(s) for this pattern of recovery is unknown. It is possible that the pattern would have been similar for other anaerobic bacteria had there been a sufficient number of isolates to permit a valid statistical comparison. Even without such data, however, it could be hypothesized that Standard Anaerobic/F bottles may provide a stricter anaerobic environment, thereby increasing the rate of recovery of strict anaerobes. This hypothesis is supported by the observation that there was a trend toward superior recovery of strict aerobes in Plus Anaerobic/F bottles.

The superior recovery from Plus Anaerobic/F bottles paral-

els that reported for other blood culture bottles containing resins or similar additives (2, 9, 10, 18, 22, 24). In controlled clinical trials these additives have been shown to improve microbial recovery, particularly for staphylococci (10, 20, 24, 25, 26, 28, 29). The mechanism(s) by which these additives increase microbial recovery is unknown. With the earlier BACTEC systems (e.g., BACTEC 460, 660, 730, and 860), one postulated mechanism of increased recovery was mechanical cell lysis caused by rapid agitation and a shearing effect of the glass beads within the broth medium (D. L. Jungkind, M. Thakur, and J. Dyke, Abstr. 89th Annu. Meet. Am. Soc. Microbiol. 1989, abstr. C 225, p. 431, 1989). Because continuous

TABLE 6. Comparative recovery of contaminants from BACTEC Plus Anaerobic/F and Standard Anaerobic/F blood culture bottles

Microorganism	No. of contaminants recovered from:			P
	Both bottles	Plus Anaerobic/F bottles only	Standard Anaerobic/F bottles only	
Gram-positive cocci				
Coagulase-negative staphylococci	113	168	59	<0.001
Enterococci ^a	3	1	8	<0.05
Other gram-positive cocci ^b	4	14	9	NS ^c
<i>Propionibacterium</i> spp.	1	0	14	<0.001
Other microorganisms ^d	4	6	18	NS
All microorganisms	125	189	108	<0.001

^a Includes 13 *Enterococcus faecalis* isolates and 1 *Enterococcus faecium* isolate.

^b Includes 16 viridans group streptococci, 8 *Staphylococcus aureus* isolates, and 3 nonhemolytic streptococci.

^c NS, not significant ($P > 0.050$).

^d Includes seven diphtheroids, five anaerobic diphtheroids, three *Bacillus* spp., two *Corynebacterium* spp., two *Lactobacillus* spp., two *Propionibacterium acnes* isolates, two *Veillonella parvula* isolates, one *Clostridium paraputrificum* isolate, one *Peptostreptococcus* sp., one *Bacteroides intermedius* isolate, one *Lactobacillus acidophilus* isolate, and one yeast whose species was not determined.

monitoring blood culture systems use a more gentle agitation mechanism, this mechanism of cellular lysis may not account for increased microbial recovery. There are only limited data to support an alternative hypothesis, namely, that these products bind to and inactivate antimicrobial agents within blood specimens. Data that support this hypothesis come from studies that have demonstrated increased recovery of staphylococci from patients receiving antistaphylococcal therapy (29). In the current study, such an effect was seen with *Staphylococcus aureus* and coagulase-negative staphylococci, but it was also seen with members of the family *Enterobacteriaceae* and all microorganisms combined. It also has been hypothesized that resins and other similar products bind to and inactivate non-specific inhibitory factors in blood, thereby improving microbial recovery, but there are no published data to support this hypothesis. Moreover, any assessment of the effect on non-specific inhibitors in blood needs to be separated from that of sodium polyanetholesulfonate, the anticoagulant used in BACTEC and most other commercial blood culture bottles. This agent inactivates lysozyme and complement, but it is not known whether this characteristic improves microbial recovery. Thus, the reason(s) for the pattern of increased recovery seen with resins and other similar products remains enigmatic.

Even though paired Plus Aerobic/F and Plus Anaerobic/F bottles showed enhanced yields in this study, whether or not use of such bottles is cost-effective or is an optimal diagnostic strategy has yet to be determined. First, Plus Aerobic/F and Plus Anaerobic/F bottles cost more than standard bottles. Because up to 90% of blood cultures are negative, much of the higher cost of Plus Aerobic/F and Plus Anaerobic/F bottles would not be offset by incremental gains in microbial recovery or improved patient care. Second, resin-containing bottles have been shown to yield more contaminants (10, 12, 25). Increased recovery of contaminants results in increased patient care and laboratory costs, offsetting, in part, any advantage of increased microbial recovery (1). Last, conclusions regarding the relative cost-effectiveness of different blood culture bottles or systems must be based on data collected specifically for that purpose.

Increased recovery of microorganisms from Plus Aerobic/F and Plus Anaerobic/F bottles for patients receiving antimicrobial therapy at the time of culture was also observed during this study. One possible explanation for this observation is that resins bind to and inactivate antimicrobial agents present in blood. In another study, the most pronounced increase in recovery was for patients with *Staphylococcus aureus* bacteremia who were receiving specific antistaphylococcal therapy at the time of culture (29). In this study, in addition to the observed increase in the rate of recovery of staphylococci, there was increased rate of recovery of members of the family *Enterobacteriaceae* and all microorganisms combined. Moreover, this pattern of recovery did not occur for patients who were not receiving antimicrobial therapy at the time of culture. Although the best explanation is that resins bind to and inactivate antimicrobial agents in blood, much remains to be explained about the pattern of increased recovery observed when media containing resins are used.

In summary, data from the present study demonstrate that microbial recovery from paired Plus Aerobic/F and Anaerobic/F bottles is superior to that from paired Plus Aerobic/F and

Standard Anaerobic/F bottles. What has yet to be demonstrated is whether this enhanced recovery offsets the higher cost of Plus Aerobic/F and Plus Anaerobic/F bottles or whether use of an alternative companion bottle (8) is a better strategy for the recovery of pathogenic bacteria and fungi from blood.

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