JOURNAL OF CLINICAL MICROBIOLOGY, Apr. 2011, p. 1624–1627 Vol. 49, No. 4
0095-1137/11/$12.00 doi:10.1128/JCM.01958-10

Comparison of BD Bactec Plus Blood Culture Media to VersaTREK Redox Blood Culture Media for Detection of Bacterial Pathogens in Simulated Adult Blood Cultures Containing Therapeutic Concentrations of Antibiotics▽

Nancy S. Miller,[1,3]* Dagmar Rogan,[1] Beverley L. Orr,[1] and Dana Whitney[2]

Department of Pathology and Laboratory Medicine[1] and Department of Pharmacy,[2] Boston Medical Center, and Boston University School of Medicine,[3] Boston, Massachusetts 02118

Received 27 September 2010/Returned for modification 8 November 2010/Accepted 27 January 2011

Antibiotic neutralization in blood culture media from two automated systems was evaluated by measuring the recovery of organisms and times to detection in simulated cultures. Overall, BD Bactec Plus media (Bactec FX system) outperformed TREK 80 ml Redox media (VersaTREK system), although results suggest a relative rather than an absolute increased rate of recovery for the Bactec media.

Blood samples taken from patients on antibiotic therapy can delay or prevent the detection of bacteremia in automated blood culture systems. BD Bactec Plus media on the new Bactec FX and the incumbent 9000 series blood culture systems (BD Diagnostics, Sparks, MD) utilize cationic-exchange and adsorbent nonionic resins to remove antibiotics from blood samples. In contrast, 80 ml Redox media on the VersaTREK blood culture system (TREK Diagnostics, Cleveland, OH) rely on an optimal 1:9 blood-broth dilution to neutralize antibiotic effects. Few recent studies (1, 2, 3) have compared VersaTREK media to Bactec media for antibiotic inactivation. This *in vitro* study compared the abilities of both systems and all media to neutralize various antibiotics at simulated trough (T), midlevel (M), and peak (P) therapeutic concentrations in serum when tested against susceptible bacterial challenge organisms.

Bactec Plus Aerobic/F (30 ml) (Bactec) media and TREK 80A aerobic Redox 1 (80 ml) (TREK) media were used for all challenge organisms. Bactec Plus Anaerobic/F (25 ml) media and TREK 80N anaerobic Redox 2 media (80 ml) were also used for *Streptococcus oralis* and *Streptococcus pneumoniae.* Stock solutions of each antibiotic (0.1 ml) were potency adjusted to simulate T, M, and P concentrations in serum based on 10 ml of blood per medium bottle. Antibiotics were chosen for clinical relevance, and serum concentrations were based on current dosing recommendations. The antibiotics tested (final T, M, and P concentrations, respectively, in μg/ml) were as follows: ampicillin (3, 12, 47), cefepime (4, 19, 164), ceftriaxone (15, 46, 250), levofloxacin (1.3, 4.5, 12), piperacillin-tazobactam (1.4-0.2, 16-2, 298-37), and vancomycin (10, 25, 50). These were tested against ATCC challenge strains as indicated in Tables 1 and 2. Concentrations for each antibiotic were per the manufacturer or calculated from the antibiotic's half-life and based on recommended doses for the treatment of severe infections in an average-weight adult with normal renal function. A susceptible MIC for each antibiotic was confirmed by replicate testing using the Etest agar gradient method (bioMérieux SA) for each relevant bacterial species tested against that drug. Medium bottles were inoculated with 10 ml banked whole blood (Interstate Blood Bank, Inc., Memphis, TN) that was not more than 5 days old, 0.1 ml potency-adjusted antibiotic (or saline for controls), and 0.1 ml challenge organism suspended in 0.85% saline containing between 10 and 100 CFU (inocula were confirmed by colony count plating). Inoculated bottles were incubated per the 5-day protocol on the respective instruments. Each organism/antibiotic concentration was run concurrently in triplicate for a total of two trial replications on two separate days. Antibiotic neutralization was measured as the percent recovery of organisms and time to detection (TTD) in seeded, antibiotic-containing blood culture bottles. Data are reported as aggregate results from all trials and were analyzed using SAS software (SAS Institute, Cary, NC). Organism recoveries were compared using Fisher's exact test, with a P value of <0.05 indicating statistical significance.

The overall percent recovery of organisms with Bactec media was 57.8% (198/342 bottles), and that with TREK media was 16.9% (58/342 bottles). This difference was statistically significant ($P < 0.0001$). Results were further stratified by medium type and antibiotic concentrations (Table 1). Differences were statistically significant in favor of Bactec. There were no instances in which both systems performed equally well at recovering challenge organisms for all concentrations of a specific antibiotic (Table 2). Significant differences between the two systems were observed for specific concentrations of agents. For all concentrations of vancomycin, organism recoveries with Bactec media were significantly different since no challenge organisms, including *Staphylococcus aureus*, were recovered with TREK media. For all concentrations of ceftriaxone, both systems failed to recover any *Streptococcus pneumoniae* or *Streptococcus oralis* organisms despite their acceptable growth in control bottles. Results are further tabulated in Table 2.

* Corresponding author. Mailing address: Division of Laboratory Medicine, Boston Medical Center, 88 East Newton Street, H3600, Boston, MA 02118. Phone: (617) 638-8705. Fax: (617) 638-4556. E-mail: nancy.miller@bmc.org.

▽ Published ahead of print on 9 February 2011.

TABLE 1. Overall organism recovery and average TTD by medium type and antibiotic concentrations

Medium	Drug (T, M, P concn)[a]	Statistic[b]	Total no. of bottles	No. of bottles with indicated Bactec result (% of bottles)				No. of bottles with indicated TREK result (% of bottles)				*P* value for:			
				Control	Trough	Midlevel	Peak	Control	Trough	Midlevel	Peak	Control	Trough	Midlevel	Peak
Aerobic		Recovered	84	84 (100)	65 (77.4)	50 (59.5)	33 (39.3)	84 (100)	35 (41.7)	10 (11.9)	2 (2.4)	1.000	<0.001	<0.001	<0.001
		Avg TTD		12.6	18	20.9	23	12.7	20.1	38.2	21.3				
		Combined				148/252 (58.7)				47/252 (18.6)					
Anaerobic		Recovered	30	30 (100)	19 (63.3)	16 (53.3)	15 (50)	29 (96.7)	6 (20)	5 (16.7)	0 (0)	1.000	<0.001	0.006	<0.001
		Avg TTD		11.8	18	25	30	15.8	14.8	47.4	NA[c]				
		Combined				50/90 (55.5)				11/90 (12.2)					
		Overall	114	114 (100)		198/342 (57.8)		113 (99.1)		58/342 (16.9)					
Aerobic	Ampicillin (3, 12, 47)	Recovered	9	9 (100)	9 (100)	6 (66.7)	3 (33.3)	9 (100)	4 (44.4)	0 (0)	1 (11.1)	1.000	0.029	0.009	0.577
		Avg TTD		11.3	16.2	20.9	21.8	11.8	25.1	NA	30.7				
Anaerobic		Recovered	6	6 (100)	4 (66.7)	1 (16.7)	0 (0)	5 (83.3)	0 (0)	0 (0)	0 (0)	1.000	0.061	1.000	1.000
		Avg TTD		11.3	21.1	63.8	NA	16.4	NA	NA	NA				
Aerobic	Cefepime (4, 19, 164)	Recovered	12	12 (100)	6 (50)	3 (25)	0 (0)	12 (100)	6 (50)	0 (0)	0 (0)	1.000	1.000	0.217	1.000
		Avg TTD		13.6	20.8	32	NA	12.8	33.4	NA	NA				
Aerobic	Ceftriaxone (15, 46, 250)	Recovered	9	9 (100)	0 (0)	0 (0)	0 (0)	9 (100)	0 (0)	0 (0)	0 (0)				
		Avg TTD		12.1	NA	NA	NA	13.3	NA	NA	NA				
Anaerobic		Recovered	9	9 (100)	0 (0)	0 (0)	0 (0)	9 (100)	0 (0)	0 (0)	0 (0)				
		Avg TTD		12.5	NA	NA	NA	17.6	NA	NA	NA				
Aerobic	Levofloxacin (1.3, 4.5, 12)	Recovered	18	18 (100)	14 (77.8)	10 (55.6)	7 (38.9)	10 (100)	13 (72.2)	8 (44.4)	0 (0)	1.000	1.000	0.740	0.008
		Avg TTD		13.5	14.7	16	12.2	13.6	18.6	37.2	NA				
Anaerobic		Recovered	6	6 (100)	6 (100)	6 (100)	6 (100)	6 (100)	6 (100)	5 (83.3)	0 (0)	1.000	1.000	1.000	0.002
		Avg TTD		11.6	11	11.3	11.6	13.1	14.8	47.4	NA				
Aerobic	Piperacillin-tazobactam (1.4-0.2, 16-2, 298-37)	Recovered	12	12 (100)	12 (100)	9 (75)	4 (33.3)	12 (100)	12 (100)	2 (16.7)	0 (0)	1.000	1.000	0.012	0.093
		Avg TTD		14.3	14.2	16.9	16.9	13.2	13.5	42.4					
Aerobic	Vancomycin (10, 25, 50)	Recovered	24	24 (100)	24 (100)	22 (91.7)	19 (79.2)	24 (100)	0 (0)	0 (0)	1 (4.2)	1.000	<0.001	<0.001	<0.001
		Avg TTD		11.2	21.7	23.3	28.4	11.9	NA	NA	11.9				
Anaerobic		Recovered	9	9 (100)	9 (100)	9 (100)	9 (100)	9 (100)	0 (0)	0 (0)	0 (0)				
		Avg TTD		11.7	21.3	29.8	42.2	15.4	NA	NA	NA				

[a] Antibiotic concentrations (μg/ml) at trough, midlevel, and peak.

[b] "Recovered" means the number of bottles from which organisms were recovered. TTDs are in hours (values are rounded to the nearest decimal). "Combined" means the summed number of T, M, and P bottles in which organisms were recovered/total number of bottles tested.

[c] NA, not applicable (no organism growth in any bottles).

TABLE 2. Microorganism-specific recovery by antibiotic concentration

Drug	Microorganism[a]	Total no. of bottles	Antimicrobial concn (μg/ml) or no. (%) of bottles positive at indicated concn with:					
			Bactec media			TREK media		
			Trough	Midlevel	Peak	Trough	Midlevel	Peak
Ampicillin			3	12	47	30	12	47
	Streptococcus pneumoniae	6	6 (100)	1 (16.7)	0 (0)	0 (0)	0 (0)	0 (0)
	Streptococcus oralis	6	4 (66.7)	3 (50)	1 (16.7)	1 (16.7)	0 (0)	0 (0)
	Enterococcus faecalis	3	3 (100)	3 (100)	2 (66.7)	3 (100)	0 (0)	1 (33.3)
Cefepime			4	19	164	4	19	164
	Escherichia coli	6	1 (16.7)	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)
	Pseudomonas aeruginosa	6	5 (83.3)	3 (50)	0 (0)	5 (83.3)	0 (0)	0 (0)
Ceftriaxone			15	46	250	15	46	250
	Streptococcus pneumoniae	6	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Streptococcus oralis	12	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Levofloxacin			1.3	4.5	12	1.3	4.5	12
	Streptococcus pneumoniae	12	12 (100)	12 (100)	12 (100)	12 (100)	11 (91.7)	0 (0)
	Escherichia coli	6	2 (33.3)	0 (0)	0 (0)	1 (16.7)	0 (0)	0 (0)
	Pseudomonas aeruginosa	6	6 (100)	4 (66.7)	1 (16.7)	6 (100)	2 (33.3)	0 (0)
Piperacillin-tazobactam			1.4-0.2	16-2	298-37	1.4-0.2	16-2	298-37
	Escherichia coli	6	6 (100)	5 (83.3)	3 (50)	6 (100)	2 (33.3)	0 (0)
	Pseudomonas aeruginosa	6	6 (100)	4 (66.7)	1 (16.7)	6 (100)	0 (0)	0 (0)
Vancomycin			10	25	50	10	25	50
	Staphylococcus aureus MSSA	6	6 (100)	4 (66.7)	1 (16.7)	0 (0)	0 (0)	0 (0)
	Staphylococcus aureus MRSA	6	6 (100)	6 (100)	6 (100)	0 (0)	0 (0)	0 (0)
	Streptococcus pneumoniae	6	6 (100)	6 (100)	6 (100)	0 (0)	0 (0)	0 (0)
	Streptococcus oralis	12	12 (100)	12 (100)	12 (100)	0 (0)	0 (0)	0 (0)
	Enterococcus faecalis	3	3 (100)	3 (100)	3 (100)	0 (0)	0 (0)	1 (33.3)

[a] Microorganism and ATCC catalog numbers are as follows: *Streptococcus pneumoniae* ATCC 49619, *Streptococcus oralis* ATCC 10557, *Enterococcus faecalis* ATCC 49533, *Staphylococcus aureus* ATCC 25923 (MSSA), *Staphylococcus aureus* ATCC 43300 (methicillin-resistant *S. aureus* [MRSA]), *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 27853.

Results showed Bactec Plus media to be significantly more efficient at recovering challenge organisms in the presence of antibiotics than TREK Redox media. For both systems, when percent organism recovery was not 100%, it decreased with increasing amounts of antibiotic, consistent with expectations (4, 6, 11). (Two outliers of this finding are evident in Table 2 for TREK media; for ampicillin, there was recovery of *Enterococcus faecalis* at trough and peak concentrations but not at the midlevel concentration, and for vancomycin, there was recovery of *E. faecalis* only at the peak concentration of vancomycin. For each of these apparent paradoxes, the possibility of a clerical error or variation in bottle inoculation [pipetting] cannot be excluded).

The current study design intentionally mirrored one used by Flayhart et al. (4) for their comparison of Bactec and BacT/Alert medium, but we used the Bactec FX instrument and the 30-ml Plus Aerobic/F bottle (instead of the model 9240 cabinet and 25-ml Plus Aerobic/F bottle); slightly different T, M, and P concentrations of antibiotics in serum were based on our clinical pharmacist's calculations. Our results are similar to those reported by Flayhart et al. However, the overall recovery of organisms with Bactec media (68.4%) and recovery of organisms from test bottles (57.8%) in this study differ from those of Flayhart et al. (95.1% and 93.4%, respectively) and are likely attributable to differences in MICs or the numbers of organisms or antibiotics used. Where calculated serum concentrations were the same and results could be equitably compared, both our study and that of Flayhart et al. showed equivalent or enhanced recoveries of organisms with Bactec media versus the comparator system (4). Notable variations in Bactec medium performance between the two studies include recoveries of *S. pneumoniae* in the presence of ampicillin, *S. aureus* (methicillin-susceptible *S. aureus* [MSSA]) in the presence of vancomycin, and *Escherichia coli* and *Pseudomonas aeruginosa* in the presence of cefepime. In each instance, higher percentages of organisms were recovered with Bactec media in the study of Flayhart et al. than in the present study. However, in our study, more *S. pneumoniae* organisms were recovered with Bactec media in the presence of vancomycin than in the study of Flayhart et al. We used lower calculated midlevel antibiotic concentrations than did Flayhart et al., but our recovery rates with Bactec media were lower. These differences are possibly due to variations in inoculum at extremes of the allowed range or differences in antibiotic MICs (data were unable to be compared). In the present study, Bactec media also provided an advantage over TREK media with regard to overall TTD (Table 1). A delay in detection time was generally dependent on an increased concentration of antibiotic, consistent with the results of other studies (8, 10). Divergent results seem to be due to a majority of isolates not growing within 5 days at the higher drug concentration.

LaBombardi et al. (6) also noted discrepancies between

their own incomplete resin adsorption results and the results of other reports citing apparent resin binding and successful organism recovery, including those cited by Flayhart et al. Results for simulated studies (4, 9, 10) are not always concordant with those of controlled clinical trials (5, 7, 12), but two seeded studies (1, 3) and one limited prospective study (2) have favored Bactec media over TREK media in their respective scenarios of antibiotic or other antimicrobial neutralization.

Simulated trials do not account for any advantages that might be conferred to TREK media by patient serum-related antibiotic-neutralizing factors in the context of broth dilution; to date, this has not been thoroughly evaluated by controlled clinical studies. Our findings suggest a relative rather than an absolute advantage for the Bactec system compared to the TREK system, within the limitations of a simulated study. The time of draw for blood cultures should remain an important clinical consideration to ensure that samples are taken at the lowest possible levels of antibiotics in serum in order to facilitate optimal recovery of bloodstream pathogens.

We acknowledge Christopher Amantia and his colleagues in the BMC Clinical Microbiology Laboratory for their technical help in conducting this study. We thank Gheorghe Doros (Boston University Department of Biostatistics) for his analysis of the study data.

Material support for this study was provided by BD Diagnostics, Sparks, MD.

We report no conflict of interest.

REFERENCES

1. **Dam, L. M., et al.** 2010. Comparison of the BACTEC Plus blood culture media to the VersaTREK REDOX blood culture media for detection of yeast in seeded blood culture specimens containing therapeutic levels of antifungal agents, abstr. C-2066. Abstr. 110th Gen. Meet. Am. Soc. Microbiol., San Diego, CA. American Society for Microbiology, Washington, DC.
2. **DiPersio, J., and H. Bonilla.** 2010. Comparison of BACTEC Plus Aerobic/F and VersaTREK REDOX 1 blood culture media for the recovery of *S. aureus* from patients with suspected persistent bacteremia, abstr. C-1134. Abstr. 110th Gen. Meet. Am. Soc. Microbiol., San Diego, CA. American Society for Microbiology, Washington, DC.
3. **DiPersio, J., L. DiPersio, and J. Beach.** 2008. Recovery of *Staphylococcus aureus* from BACTEC PLUS and VersaTrek REDOX 1 blood culture media with increasing concentrations of vancomycin, daptomycin, or linezolid, abstr. D-306. Abstr. 48th Annu. Intersci. Conf. Antimicrob. Agents Chemother. (ICAAC)-Infect. Dis. Soc. Am. (IDSA) 46th Annu. Meet. American Society for Microbiology and Infectious Diseases Society of America, Washington, DC.
4. **Flayhart, D., A. P. Borek, T. Wakefield, J. Dick, and K. C. Carroll.** 2007. Comparison of BACTEC PLUS blood culture media to BacT/Alert FA blood culture media for detection of bacterial pathogens in samples containing therapeutic levels of antibiotics. J. Clin. Microbiol. **45:**816–821.
5. **Jorgensen, J. H., et al.** 1997. Controlled clinical laboratory comparison of BACTEC Plus Aerobic/F resin medium with BacT/Alert aerobic FAN medium for detection of bacteremia and fungemia. J. Clin. Microbiol. **35:**53–58.
6. **LaBombardi, V., J. Sotos, S. Allen, and N. Sullivan.** 2009. Resins do not adsorb all antibiotics at peak serum concentrations, especially the newer beta-lactam antibiotics, abstr. C-048. Abstr. 109th Gen. Meet. Am. Soc. Microbiol., 17 to 21 May 2009, Philadelphia, PA. American Society for Microbiology, Washington, DC.
7. **Pohlman, J. K., B. A. Kirkley, K. A. Easley, B. A. Basille, and J. A. Washington.** 1995. Controlled clinical evaluation of BACTEC Plus aerobic/F and BacT/Alert aerobic FAN bottles for detection of bloodstream infections. J. Clin. Microbiol. **33:**2856–2858.
8. **Spaargaren, J., C. P. A. van Boren, and G. P. Voorn.** 1998. Effectiveness of resins in neutralizing antibiotic activities in BACTEC Plus Aerobic/F culture medium. J. Clin. Microbiol. **36:**3731–3733.
9. **Vigano, E. F., E. Vasconi, C. Agrappi, and P. Clerici.** 2002. Use of simulated blood cultures for time to detection comparison between BacT/ALERT and BACTEC 9240 blood culture systems. Diagn. Microbiol. Infect. Dis. **44:**235–240.
10. **Vigano, E. F., E. Vasconi, C. Agrappi, P. Clerici, and P. Melloni.** 2004. Use of simulated blood cultures for antibiotic effect on time to detection of the two blood culture systems BacT/Alert and BACTEC 9240. New Microbiol. **27:**235–248.
11. **Washington, J. A., II, and D. M. Ilstrup.** 1986. Blood cultures: issues and controversies. Rev. Infect. Dis. **8:**792–802.
12. **Ziegler, R., I. Johnscher, P. Martus, D. Lenhardt, and H.-M. Just.** 1998. Controlled clinical laboratory comparison of two supplemented aerobic and anaerobic media used in automated blood culture systems to detect bloodstream infections. J. Clin. Microbiol. **36:**657–661.