JOURNAL OF CLINICAL MICROBIOLOGY, Feb. 2007, p. 299–302 Vol. 45, No. 2
0095-1137/07/$08.00+0 doi:10.1128/JCM.01697-06

Controlled Clinical Comparison of VersaTREK and BacT/ALERT Blood Culture Systems▽

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Received 16 August 2006/Returned for modification 11 October 2006/Accepted 8 November 2006

To assess the relative yields in automated microbial detection systems of bacteria and yeasts isolated from the blood of adult patients with suspected sepsis, we compared the new VersaTREK system (VTI) (TREK Diagnostic Systems, Cleveland, OH) to the BacT/ALERT 3D system (3D) (bioMérieux, Inc., Durham, NC). Identical protocols were followed for the two systems. Paired aerobic (REDOX 1) and anaerobic (REDOX 2) VTI media were compared with standard aerobic (SA) and anaerobic (SN) 3D media; each of the four culture bottles was filled with 6 to 9 ml of blood. All bottles flagged positive by the instruments were subcultured to determine both true-positive (growth) and false-positive (no growth) cultures. Additionally, to assess false-negative bottles, terminal subcultures were done on all negative companion bottles to true-positive bottles. All isolates were identified by standard methods. All 4 bottles were adequately filled and yielded 413 clinically significant isolates in 5,389 (79%) of the 6,786 4-bottle sets obtained. Although no overall difference in yield or in time to detection was detected between the two systems, significantly more streptococci and enterococci as a group were detected by VTI. Moreover, significantly more microorganisms were detected by VTI for patients receiving antimicrobial therapy. The two systems were comparable (*P*, not significant) at detecting the 179 unimicrobial episodes of bacteremia seen. False-positive rates for aerobic and anaerobic bottles, respectively, were 1.6% and 0.9% for VTI and 0.7% and 0.8% for 3D. We conclude that the VTI and 3D systems are comparable for detection of bloodstream infections with bacteria or yeasts.

Two of the three automated microbial detection systems approved for use in the United States for the detection of bacteremia and fungemia are VersaTREK (VTI) (TREK Diagnostic Systems, Cleveland, OH) and BacT/ALERT 3D (3D) (bioMérieux, Durham, NC). The VersaTREK automated microbial detection system evolved from and replaced the Difco ESP culture II system; it was commercially introduced in 2003. The detection of positive cultures by VTI is based on measuring pressure changes in the bottle headspace (due to consumption and production of gas by the microorganism) with an external pressure sensor, whereas the BacT/ALERT automated microbial detection system uses an internal colorimetric sensor for the detection of CO_2 produced by microbial metabolism. Additional differences between the systems include the composition of the media, the concentration or type of anticoagulant, and the volume of broth in the bottles designed for the respective systems. Furthermore, the VTI aerobic bottle uses a stir bar that creates a vortex within the bottle, whereas the anaerobic bottle is neither shaken nor stirred. This procedure differs from that of 3D, which uses a rocking motion for all bottles. The net result of these differences between VTI and 3D in actual performance has not been evaluated in a controlled clinical trial. Therefore, we compared the two systems for detection of bacteremia and fungemia in the blood of adult patients with suspected sepsis.

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▽ Published ahead of print on 22 November 2006.

MATERIALS AND METHODS

Background information. The study was conducted at the Duke University Medical Center between November 2003 and August 2004. Institutional Review Board approval was obtained before the start of the study, and blood cultures were drawn from adult patients with suspected bacteremia or fungemia upon physician request as part of routine patient care.

Blood culture collection. Venipuncture sites were disinfected with 10% povidone-iodine followed by 70% isopropyl alcohol. Thirty milliliters of blood was withdrawn using sterile needles and syringes or, if necessary, a blood collection set for a direct draw via a butterfly needle and direct inoculation into blood culture bottles. Once drawn, 7.5 ml of blood was randomly distributed, through a device designed for safe transfer of blood, into both VTI aerobic (REDOX 1) and anaerobic (REDOX 2) bottles (TREK Diagnostics, Cleveland, OH) and 3D aerobic (SA) and anaerobic (SN) standard bottles (bioMérieux, Durham, NC). Instructions for the order in which bottles were to be inoculated were provided with each kit. The order was changed after each 1,000 kits distributed. Inoculated bottles were then labeled and transported to the microbiology laboratory.

Laboratory processing. Cultures were accessioned by the laboratory's routine procedure. Each bottle was compared with prefilled volume standards, and the volume was recorded. Bottles were categorized as underfilled (<6 ml), adequately filled (6 to 9 ml), or overfilled (>9 ml). All bottles containing any volume of blood were processed for purposes of patient care, and analyses were performed both for adequately filled bottles (e.g., bottles containing 6 to 9 ml of blood) and for bottles filled regardless of adequacy. Upon receipt, bottles were placed in the respective instruments.

Bottle incubation and testing were performed according to each manufacturer's recommendations. Bottles were incubated either until they were flagged as positive or for 5 days. Bottles flagged as positive were removed from the instruments. An aliquot of the blood-broth mixture within each instrument-positive bottle was removed aseptically using a needle and syringe. Part of each aliquot was used for Gram staining; the remaining portion was used for subculture on solid medium according to the results of the Gram stains. Isolates were identified using standard methods (4). Bottles with a negative Gram stain were returned to incubation units. After 5 days of incubation, terminal subcultures were performed on "negative" bottles from blood culture sets in which one or more other bottles from either instrument in the set were positive.

Assessment of the clinical importance of isolates. Positive blood cultures were categorized as true positives, contaminated cultures, or cultures with microor-

TABLE 1. Comparative yields of clinically important isolates from adequately filled bottles in the VTI and 3D blood culture systems

Microorganism	No. of isolates recovered from:			*P*
	Both systems	VTI only	3D only	
Gram-positive cocci				
S. aureus	43	13	5	NS[a]
Coagulase-negative staphylococci	36	5	9	NS
Streptococcus and *Enterococcus* spp.[b]	60	16	6	<0.05
Gram-negative bacilli				
Enterobacteriaceae[c]	95	17	15	NS
Nonfermenters[d]	20	3	6	NS
Anaerobic bacteria[e]	11	10	3	NS
Yeasts[f]	23	8	9	NS
All microorganisms	288	72	53	NS

[a] NS, not significant ($P > 0.05$).
[b] Includes 31 *Enterococcus faecium* isolates, 21 viridans streptococci, 18 *Enterococcus faecalis* isolates, 5 *Enterococcus avium* isolates, 5 beta-hemolytic streptococci, 1 *Streptococcus pneumoniae* isolate, and 1 *Enterococcus* sp. strain.
[c] Includes 43 *Escherichia coli*, 28 *Klebsiella pneumoniae*, 19 *Serratia marcescens*, 15 *Enterobacter cloacae*, 7 *Enterobacter aerogenes*, 6 *Proteus mirabilis*, 3 *Klebsiella oxytoca*, 2 *Citrobacter freundii*, 2 *Serratia liquefaciens*, 1 *Enterobacter taylorae*, and 1 *Salmonella enteritidis* group D isolate.
[d] Includes 16 *Stenotrophomonas maltophilia*, 11 *Pseudomonas aeruginosa*, 1 *Acinetobacter baumannii*, and 1 *Ochrobactrum anthropi* isolate.
[e] Includes nine *Bacteroides fragilis*, six *Clostridium septicum*, four *Bacteroides thetaiotaomicron/ovatus* group, two *Clostridium perfringens*, one *Bacteroides uniformis*, one *Clostridium tertium*, and one *Eubacterium lentum* isolate.
[f] Includes 14 *Candida parapsilosis*, 12 *Candida glabrata*, 9 *Candida albicans*, 4 *Candida tropicalis*, and 1 *Candida krusei* isolate.

TABLE 2. Comparative yields of clinically important isolates from adequately filled bottles for patients on antimicrobial therapy by the VTI and 3D blood culture systems

Microorganism	No. of isolates recovered from:			*P*
	Both systems	VTI only	3D only	
Gram-positive cocci				
S. aureus	6	5	4	NS[a]
Coagulase-negative staphylococci	7	3	1	NS
Streptococcus and *Enterococcus* spp.[b]	9	5	0	NS
Gram-negative bacilli				
Enterobacteriaceae[c]	15	8	4	NS
Nonfermenters[d]	7	1	0	NS
Anaerobic bacteria (*Eubacterium lentum*)	1	0	0	NS
Yeasts[e]	6	3	1	NS
All microorganisms	51	25	10	<0.025

[a] NS, not significant ($P > 0.05$).
[b] Includes six *Enterococcus faecalis*, five *Enterococcus faecium*, and two *Enterococcus avium* isolates and one beta-hemolytic streptococcus.
[c] Includes seven *Escherichia coli*, six *Klebsiella pneumoniae*, five *Serratia marcescens*, five *Enterobacter cloacae*, two *Serratia liquefaciens*, one *Proteus mirabilis*, and one *Salmonella enteritidis* group D isolate.
[d] Includes seven *Stenotrophomonas maltophilia* isolates and one *Pseudomonas aeruginosa* isolate.
[e] Includes nine *Candida parapsilosis* isolates and one *Candida albicans* isolate.

ganisms of unknown clinical significance based on the published criteria of Weinstein et al. (6). The judgments were made by infectious-disease clinicians, taking into account the patient's clinical history, physical findings, laboratory test results (including the results of cultures of specimens from other sites), imaging studies, clinical course, and response to therapy.

Data analysis. Information recorded and collated included (i) which bottle types were received with each blood culture set, (ii) the adequacy of filling of the bottles, (iii) which bottle(s) in each set grew microorganisms, (iv) the means by which bottles were found to be positive (i.e., by instrument signal or terminal subculture), (v) the time required for microbial growth to be detected, (vi) the identity and clinical importance of microbial isolates, (vii) what antimicrobial therapy, if any, patients were receiving when blood cultures were drawn, (viii) a record of false-positive bottles, (ix) a record of contamination rates for the two systems, (x) the number of septic episodes detected by each system, and (xi) whether each septic episode was unimicrobial or polymicrobial. Septic episodes were defined as detection of a clinically important (i.e., the cause of sepsis) blood culture isolate without recovery of a different microorganism during the succeeding 7-day period. If a different microorganism was recovered within 72 h, the two isolates were considered part of a polymicrobial septic episode. If a different microorganism was recovered after 72 h, the two isolates were considered to be the causes of two septic episodes. All positive cultures were included if the patient had at least one blood culture set where all four bottles were adequately filled. Data were entered into a database program (Microsoft Access), and statistical analyses were performed using the chi-square test modified with Yates' correction when n was ≤ 20 (3).

RESULTS

Overall, 7,762 blood culture sets were submitted during the study, including 5,389 (69%) with an adequate volume of blood in all four bottles and 6,786 (87%) with all four bottles received regardless of adequacy. 3D bottles were underfilled more often (892 aerobic and 638 anaerobic bottles) than VTI bottles (265 aerobic and 347 anaerobic bottles). The numbers of overfilled bottles were similar for the two systems. Of the 5,389 blood culture sets, 543 yielded 624 microorganisms, including 413 (7.7%) isolates considered to be the cause of sepsis, 148 (2.7%) contaminants, and 63 (1.2%) isolates that were indeterminate as the cause of sepsis. Table 1 shows no significant difference in the overall isolation of microorganisms between the two systems except for streptococci and enterococci as a group, which were found more frequently by VTI ($P < 0.05$). Table 2 compares the two systems for patients on therapy at the time of blood culture. VTI showed a statistically significant improvement in recovery for all microorganisms combined ($P < 0.025$) when all four bottles were filled adequately.

Table 3 compares the two systems by episode analysis. Of 209 episodes of bacteremia and fungemia detected in this evaluation, there were 179 unimicrobial episodes, which were analyzed further; 30 polymicrobial episodes were excluded from the analysis. There was no significant difference between the two systems in the detection of microbial episodes for any specific group of microorganisms or overall: 23 episodes were detected only by VTI, and 19 episodes were detected only by 3D (*P*, not significant).

Table 4 compares the mean times to detection of isolates causing bacteremia and fungemia for positive cultures detected by the two blood culture systems. Each culture was examined in order to determine which bottle gave the earliest positive result in each system. This earliest positive bottle was compared to the earliest positive bottle in the other system. The overall times to detection were similar for the two systems, despite some differences by subgroup.

Of the 148 contaminants recovered during this study, 49 were detected in both systems, 56 in VTI only, and 43 in 3D only.

More instrument false-positive readings were obtained with

TABLE 3. Comparative detection of clinically important episodes by the VTI and 3D blood culture systems

Microorganism	No. of isolates recovered from:			P
	Both systems	VTI only	3D only	
Gram-positive cocci				
S. aureus	27	2	1	NS[a]
Coagulase-negative staphylococci	19	0	1	NS
S. pneumoniae	1	0	0	NS
Streptococcus and *Enterococcus* spp.[b]	19	3	1	NS
Gram-negative bacilli				
Enterobacteriaceae[c]	45	4	6	NS
Nonfermenters[d]	6	3	4	NS
Anaerobic bacteria	6	5	3	NS
Yeasts[e]	14	6	3	NS
All microorganisms	137	23	19	NS

[a] NS, not significant ($P > 0.05$).
[b] Includes 10 *Enterococcus faecium* and 7 *Enterococcus faecalis* isolates, 4 viridans streptococci, and 2 beta- hemolytic streptococci.
[c] Includes 20 *Escherichia coli*, 10 *Serratia marcescens*, 9 *Klebsiella pneumoniae*, 6 *Enterobacter cloacae*, 3 *Enterobacter aerogenes*, 2 *Klebsiella oxytoca*, 2 *Proteus mirabilis*, 1 *Enterobacter taylorae*, 1 *Salmonella enteritidis* group D, and 1 *Serratia liquefaciens* isolate.
[d] Includes eight *Pseudomonas aeruginosa*, four *Stenotrophomonas maltophilia*, and one *Ochrobactrum anthropi* isolate.
[e] Includes seven *Candida albicans*, seven *Candida glabrata*, six *Candida parapsilosis*, two *Candida tropicalis*, and one *Candida krusei* isolate.

TABLE 4. Mean times to detection of clinically important isolates from adequately filled bottles by the VTI and 3D blood culture systems

Microorganism (no. of isolates or strains)	Mean time to detection (h) by:	
	VTI	3D
Gram-positive cocci		
S. aureus (43)	17.6	19.1
Coagulase-negative staphylococci (36)	21.6	21.0
Streptococcus and *Enterococcus* spp.[a] (60)	15.7	17.9
Gram-negative bacilli		
Enterobacteriaceae[b] (95)	15.0	15.9
Nonfermenters[c] (20)	14.9	16.2
Anaerobic bacteria[d] (11)	25.3	23.9
Yeasts[e] (23)	35.8	37.5
All microorganisms (288)	18.4	19.6

[a] Includes 23 *Enterococcus faecium* isolates, 18 viridans streptococci, 10 *Enterococcus faecalis* isolates, 5 *Enterococcus avium* isolates, 2 beta-hemolytic streptococci, 1 *Streptococcus pneumoniae* isolate, and 1 *Enterococcus* sp. strain.
[b] Includes 30 *Escherichia coli*, 20 *Klebsiella pneumoniae*, 18 *Serratia marcescens*, 12 *Enterobacter cloacae*, 5 *Enterobacter aerogenes*, 5 *Proteus mirabilis*, 2 *Citrobacter freundii*, 2 *Klebsiella oxytoca*, and 1 *Enterobacter taylorae* isolate.
[c] Includes 13 *Stenotrophomonas maltophilia*, 6 *Pseudomonas aeruginosa*, and 1 *Acinetobacter baumannii* isolate.
[d] Includes four *Clostridium septicum*, three *Bacteroides fragilis*, two *Bacteroides thetaiotaomicron/ovatus* group, one *Clostridium tertium*, and one *Eubacterium lentum* isolate.
[e] Includes 10 *Candida parapsilosis*, 4 *Candida albicans*, 5 *Candida glabrata*, and 4 *Candida tropicalis* isolates.

REDOX 1 (1.6%) and REDOX 2 (0.9%) than with SA (0.7%) and SN (0.8%).

A total of 53 isolates were detected by subculturing from negative blood culture bottles when one or more other bottles in the blood culture sets were positive (Table 5). These false-negative results were most frequent for anaerobe bottles in both systems. Most isolates (43/53) were also detected in the companion bottle by the same system, but the remaining 10 isolates were detected only by the comparison system. Moreover, 28 of the 46 isolates that failed to trigger a signal in the anaerobic bottles in either instrument were strictly aerobic microorganisms.

Table 6 provides a comparison of medium formulations for the four types of bottles studied.

DISCUSSION

This evaluation was designed to compare the new VersaTREK blood culture system with the BacT/ALERT 3D blood culture system using currently available standard medium formulations. Although the instruments and software for the two systems are significantly different from the original ESP and BacT/ALERT classic versions, respectively, the bottles and media used in this study are quite similar to those described in an earlier study (Table 6) (7). The mechanism for detection of growth in both the ESP and VTI instruments is based on changes in pressure owing to the production or consumption of gases. In contrast, both the classic and 3D versions of the BacT/ALERT instruments use a colorimetric system for detecting CO_2 production.

The role of blood volume in adult cultures in detection of microorganisms is well recognized for all systems (5); consequently, we assessed the adequacy of filling for all bottles received, and we present results only for adequately filled sets in both systems. Elimination of inadequately filled bottles in comparing systems is highlighted in this study, since not doing so would have led to the comparison of more adequately filled VTI bottles with inadequately filled 3D bottles. Despite changes in the order of inoculation of bottles, VTI bottles were more frequently adequately filled. A difference in the vacuum between VTI and 3D bottles is the most plausible explanation for this observation.

In the study reported here, we found that the performance of VTI and that of the current 3D version of the BacT/ALERT system showed substantial comparability in both yield and time to detection of positive blood cultures. This analysis was done for paired aerobic and anaerobic bottles (VTI REDOX 1 and REDOX 2 and BacT/ALERT 3D SA and SN), as intended by the manufacturers for use in their respective systems. Internal differences in performance with aerobic and anaerobic bottles in both systems showed the importance of paired bottles and of comparisons between systems and not between individual bottles.

An earlier evaluation of the VTI forerunner, ESP, showed higher yields of *Staphylococcus aureus* and anaerobic bacteria than those obtained with the BacT/ALERT standard media then used (7). This study showed similar trends but without statistically significant differences, except for streptococci and enterococci as a group. A plausible explanation for the improved recovery from the VTI system could be related to the increased dilution of inhibitory host factors or antimicrobials provided by bottles containing 80 ml of broth versus the 40 ml provided in the SA and SN

TABLE 5. Bottles flagged negative by the instrument but for which microorganisms were detected by blind terminal subculture

Microorganism	No. of bottles testing negative by each system and medium from which the indicated microorganism was detected by subculture:			
	VTI		3D	
	REDOX 1	REDOX 2	SA	SN
Gram-positive cocci				
Staphylococcus aureus	1	7	2	1
Coagulase-negative staphylococci	0	6	0	1
Enterococcus faecalis	0	1	0	0
Enterococcus faecium	0	0	1	1
Gram-negative bacilli				
Enterobacter cloacae	0	0	1	0
Klebsiella pneumoniae	0	1	0	0
Pseudomonas aeruginosa	0	0	0	4
Stenotrophomonas maltophilia	1	7	0	8
Anaerobic bacteria (*Bacteroides fragilis*)	1	0	0	0
Fungi				
Candida albicans	0	0	0	1
Candida glabrata	0	0	0	1
Candida parapsilosis	0	2	0	3
Candida tropicalis	0	0	0	2
Total by system and medium[a]	3	24	4	22
Total by system[b]	1	4	3	2

[a] Number of false-negative bottles for which the organism was detected in a companion bottle by either system.
[b] Number of false-negative bottles for which the organism was detected in a companion bottle only by the other system.

TABLE 6. Comparison of the formulations of the BacT/ALERT 3D SA and SN media with those of the VersaTREK REDOX 1 and REDOX 2 media

Ingredient	% (wt/vol) of the indicated ingredient in each medium[a]:			
	VTI		3D	
	REDOX 1	REDOX 2	SA	SN
Cysteine		0.05		
Dextrose	0.25	0.5		
Divalent salts A	0.009			
Hemin		0.0005		0.0005
Menadione				0.00005
Pancreatic digest of casein			1.7	1.36
Papaic digest of soybean meal			0.3	0.24
Polysorbate 80 (10%)		0.075		
Proteose-peptone N		1.5		
Pyridoxine HCl			0.001	0.0008
Pyruvic acid				0.08
Resazurin		0.0001		
Saponin		0.045		
Sodium chloride	0.5	0.23		
Sodium polyanetholesulfonate	0.0125		0.035	0.035
Soy-casein peptone A	2.1			
Supplement N		0.8		
Supplement O	0.33			
Trisodium citrate		0.07		
Vitamin K		0.0001		
Yeast extract	0.1	0.5		0.376

[a] REDOX 1 and REDOX 2 bottles each contained 80 ml of broth; SA and SN bottles each contained 40 ml.

3D bottles. Additional support for this explanation is provided by the analysis for patients on antimicrobial therapy (Table 2), for whom a statistically significant improvement in detection by VTI was shown for all microorganisms combined.

In addition to the comparable performance by system, we also analyzed the data by detection of episodes. Episode analysis provides a mechanism for eliminating duplicate cultures collected from patients and especially eliminates the bias that might occur from strain differences that might favor one system or the other. There was no statistically significant difference in the detection of episodes between VTI and 3D.

When both systems detected positive cultures, we compared the fastest bottle in VTI with the fastest bottle in 3D. This analysis showed a mean difference of 1.2 h between the two systems (Table 4). This difference would not seem important clinically.

The higher false-positive rate for both VTI bottles than for the two 3D bottles may, in part, be related to overfilled bottles or to user error related to temperature changes that occurred when the loading of bottles took an excessive amount of time, thereby allowing bottles already incubating to cool. Nonetheless, our false-positive rate is similar to that reported in other publications (1, 2, 7).

The value of paired bottles, aerobic and anaerobic, is shown in Table 5, where most of the microorganisms detected by terminal subculture were detected by the companion bottle. Only rarely was either system false negative when the complementary, paired aerobic and anaerobic bottles of each were considered together.

We conclude that the VTI and 3D systems with standard media are comparable for the detection of bloodstream infections with bacteria or yeasts commonly encountered in a tertiary referral hospital. Further studies comparing the utility of VTI aerobic and anaerobic media with other formulations of media, e.g., those containing charcoal or resins, are required in order to draw conclusions about the performance of VTI versus that of systems with media other than those studied here.

ACKNOWLEDGMENTS

This study was supported in part by a grant from TREK Diagnostics, Cleveland, OH.

We gratefully acknowledge the contribution of the medical and research technologists in our laboratory.

REFERENCES

1. **Doern, G. V., A. Barton, and S. Rao.** 1998. Controlled comparative evaluation of BacT/Alert FAN and ESP 80A aerobic media as means for detecting bacteremia and fungemia. J. Clin. Microbiol. **36:**2686–2689.
2. **Kirkley, B. A., K. A. Easley, and J. A. Washington.** 1994. Controlled clinical evaluation of Isolator and ESP aerobic blood culture systems for detection of bloodstream infections. J. Clin. Microbiol. **32:**1547–1549.
3. **McNemar, Q.** 1969. Psychological statistics. Wiley, New York, NY.
4. **Murray, P. R., E. J. Baron, M. A. Pfaller, F. C. Tenover, and R. H. Yolken (ed.).** 1999. Manual of clinical microbiology, 7th ed. ASM Press, Washington, DC.
5. **Weinstein, M. P.** 1996. Current blood culture methods and systems: clinical concepts, technology, and interpretation of results. Clin. Infect. Dis. **23:**40–46.
6. **Weinstein, M. P., M. L. Towns, S. M. Quartey, S. Mirrett, L. G. Reimer, G. Parmigiani, and L. B. Reller.** 1997. The clinical significance of positive blood cultures in the 1990s: a prospective comprehensive evaluation of the microbiology, epidemiology, and outcome of bacteremia and fungemia in adults. Clin. Infect. Dis. **24:**584–602.
7. **Zwadyk, P., C. L. Pierson, and C. Young.** 1994. Comparison of Difco ESP and Organon Teknika BacT/Alert continuous-monitoring blood culture systems. J. Clin. Microbiol. **32:**1273–1279.