Comparison of BD Bactec Plus Aerobic/F Medium to VersaTREK Redox 1 Blood Culture Medium for Detection of *Candida* spp. in Seeded Blood Culture Specimens Containing Therapeutic Levels of Antifungal Agents[▽]

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Recovery of *Candida* spp. using the BD Bactec FX blood culture (BC) system (Bactec Plus Aerobic/F medium) and the VersaTREK system (aerobic Redox medium) was evaluated using seeded BC bottles with and without the addition of commonly used antifungal agents. BC bottles ($n = 1,442$) were each inoculated with 10 ml human whole blood and 0.1 ml of suspensions of *Candida* spp., with or without antifungal agents. BC bottles were incubated in the corresponding system for a maximum of 5 days. In the absence of antifungal agents, Bactec FX recovered 97.4% of *Candida* spp., and VersaTREK recovered 99.1% ($P = 0.154$). With regard to length of time to detection (LTD) and overall recovery, both systems had various levels of effectiveness in recovering *C. glabrata*. In bottles containing antifungal agents, Bactec FX recovered 83.1% of isolates, whereas VersaTREK recovered 50.7% of *Candida* spp. ($P < 0.001$). For BC bottles without the addition of antifungal agents, the median LTD for VersaTREK was 2.2 h faster than that of Bactec FX ($P < 0.001$). In the presence of antifungal agents, the Bactec FX recovery time was significantly faster than that of VersaTREK (median difference of 10.8 h, $P < 0.001$). We conclude that both systems have comparable abilities to recover *Candida* spp. from seeded blood cultures in the absence of antifungal agents. In the presence of therapeutic levels of commonly used antifungal agents, the Bactec FX system demonstrated a significantly greater recovery of various *Candida* spp., as well as a shorter LTD.

Candida spp. are the ninth most common cause of bloodstream infections (BSI) and the fourth most common cause of nosocomial BSI in the United States (8, 25, 28, 31). *Candida* spp. further account for one-third of all causes of BSI in intensive care units (ICU) in the United States (34). *Candida albicans* persists as the most common cause of candidemia, and the organism remains widely susceptible to fluconazole (8). However, studies within the past 5 to 10 years have demonstrated an increase of BSIs due to non-*albicans Candida* spp., with *C. tropicalis*, *C. glabrata*, *C. krusei*, and *C. parapsilosis* being the most commonly isolated species (8, 19, 34). Together, these organisms represent approximately one-half of all *Candida* spp. isolated from blood cultures (BC) in the United States.

BSI due to non-*albicans Candida* spp. is associated with risk factors such as hospital stay in the ICU, bone marrow transplantation, cancer, immunosuppression, and HIV/AIDS. The emergence of resistance to antifungal agents has been known for several species, particularly *C. glabrata* and *C. krusei* (19, 31, 33). Candidemia impacts length of stay, cost of hospitalization, and patient mortality (18, 31). Considering a crude mortality rate of between 40% and 60%, the need for rapid and accurate diagnosis of fungemia is essential (33). Isolation

of the organism in BC, followed by antifungal susceptibility testing (AFST), has become the mainstay for providing guidance for treatment of candidemia (17). The traditional paradigm of culture-directed treatment has changed over the past decade and prophylactic or empirical treatment has now been suggested for patients at high risk for candidemia and invasive disease due to *Candida* spp. (22, 24). Empirical treatment is defined as administering antifungal therapy to patients with clinical features indicative of invasive candidiasis in the absence of culture-proven etiology. Although little evidence-based support exists for the use of empirical antifungal therapy, it is a commonly accepted practice with high-risk patients (24). Such practice may have an impact on the ability of microbiology laboratories to recover yeast from blood cultures obtained from such patients.

Candidemia is commonly detected using automated, continuous-monitoring blood culture systems (CMBCS) followed by the use of standard laboratory agar media for subculturing positive BC bottles. However, the sensitivity of these systems for detection of candidemia has been questioned in recent years (3, 14, 15, 30). Terminal subcultures of signal-negative BC bottles at the end of a routine incubation cycle (5 days) have demonstrated no significant improvement for the detection of candidemia (28). A few studies investigated the performance of CMBCS for the detection of candidemia by the use of the Bactec 9240 system (BD Diagnostics, Sparks, MD) and the BacT/Alert system (bioMérieux, Inc., Durham, NC) (14–16, 26). To our knowledge, only one study has been published of a comparison of the VersaTREK system (Trek Diagnostic

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TABLE 1. Antifungal susceptibility test results (MIC ranges and MIC₉₀) for selected *Candida* spp.^b

<i>Candida</i> sp. (no. of isolates tested)	MIC range/MIC ₉₀ ^a (μg/ml)			
	Amphotericin	Fluconazole	Voriconazole	Caspofungin
<i>C. albicans</i> (10)	0.25–0.5/0.5	<0.125–0.5/0.5	<0.008–0.016/0.008	0.016–0.25/0.25
<i>C. glabrata</i> (4)	0.25–1.0/0.5	16/16	0.25–0.5/0.5	0.06–0.25/0.25
<i>C. tropicalis</i> (3)	0.5–1.0/1	0.5–1.0/1	0.016–0.06/0.06	0.03–0.25/0.25
<i>C. parapsilosis</i> (2)	0.25–1.0	1.0–4.0	<0.008–0.06	0.25–0.5

^a The MIC₉₀ was not calculated if the number of isolates was <3.

^b ATCC and clinical isolates as listed in Materials and Methods.

Systems, Cleveland, OH) and the BacT/Alert system for the ability to recover microorganisms from blood cultures (20). No trials have been published comparing the VersaTREK system to other systems, nor have any trials examined the VersaTREK's ability to detect candidemia.

In this present study, we compared the performance of Bactec Plus Aerobic/F blood culture medium (Bactec FX system) to that of VersaTREK Redox 1 blood culture medium (VersaTREK system) for detection of *Candida* spp. in seeded blood culture specimens with and without therapeutic levels of antifungal agents.

(This work was presented in part at the 110th General Meeting of the American Society for Microbiology, San Diego, CA [7]).

MATERIALS AND METHODS

This research study was approved by the Institutional Review Board of the Johns Hopkins Medical Institutions. Between December 2009 and April 2010, we tested a total of 1,442 seeded blood culture bottles for the CMBCS (VersaTREK system [*n* = 721]) and Bactec FX system (*n* = 721). We evaluated their ability to detect *Candida* spp. in BC bottles with and without the presence of select antifungal agents at therapeutic peak and trough drug levels.

***Candida* spp. used for testing.** The *Candida* spp. used for this study were originally obtained from unique patients with proven fungemia as detected by our laboratory's clinical CMBCS (VersaTREK system) and stored frozen (–70°C) until tested. The isolates recovered were *C. albicans* (9), *C. glabrata* (3), *C. tropicalis* (3), and *C. parapsilosis* (1). In addition, one isolate of each of the following type strains of *Candida* spp. was used: *C. albicans* (ATCC 60193), *C. glabrata* (ATCC 15126), *C. tropicalis* (ATCC 1369), and *C. parapsilosis* (ATCC 22029). All previously frozen stored isolates were subcultured twice on BBL Sabouraud dextrose agar (Emmons) (BD Diagnostics, Sparks, MD) before use in the seeding experiments to ensure viability and purity. During the initial phase of the study, one isolate of *C. krusei* (ATCC 14243), one isolate of *Cryptococcus laurentii* (ATCC 18803), and three clinical isolates of *Cryptococcus neoformans* were included for setup of testing. The results for these 5 isolates were subsequently eliminated from the data analysis because of the small number of isolates and the consistently poor growth in the aerobic blood culture bottles.

Antifungal agents used for testing. All isolates were tested against the following commonly used antifungal agents at both peak- and trough-level concentrations: amphotericin B (AMB), fluconazole (FCA), voriconazole (VOR), and caspofungin (CAS). Antifungal susceptibility testing using the Sensititre Yeast-One system (Trek Diagnostics, Cleveland, OH) was performed on all isolates prior to the seeding experiments. Susceptibility testing was performed according to the manufacturer's recommendations (29) and established clinical laboratory practices, as well as established guidelines for interpretation of antimicrobial susceptibility testing (AST) (4). All isolates tested susceptible or susceptible-dose dependent (fluconazole and *C. glabrata*) to the above-referenced antifungal agents (Table 1).

Antifungal agents used for inoculating BC bottles were purchased from the respective manufacturer(s), and peak and trough concentrations were prepared according to published guidelines for these levels (1, 2). Peak- and trough-level stock solutions for AMB and FCA were prepared and then stored at –20°C until further use for inoculation in BC bottles. Corresponding stored tubes with antifungal agents were thawed within 1 h prior to use.

Peak-level solutions for AMB were prepared by adding 8 ml of a 250-μg/ml AMB stock solution to 2 ml of sterile distilled water (dH₂O) to create 10 ml of

a 200-μg/ml stock. A corresponding 0.1-ml inoculum of this solution contained 20 μg of AMB, corresponding to the approximate amount of drug present in 10 ml of blood. Trough-level solutions were prepared by adding 2 ml of a 250-μg/ml AMB stock solution to 8 ml of sterile dH₂O, creating 10 ml of a 50-μg/ml stock. A 0.1-ml inoculum of this solution contained 5 μg of AMB, corresponding to the amount of drug present in 10 ml of blood.

In brief, following the same principle for dilution in dH₂O, stock solutions for the peak level and trough level were prepared from an original 2,350-μg/ml FCA stock solution. Fourteen-milliliter tubes for the FCA peak level (672 μg/ml) and 14-ml tubes for FCA at trough level (418 μg/ml) were prepared.

Voriconazole for injection (Vfend I.V.), 200 mg/vial lyophilized powder, was purchased from Pfizer, Inc., and reconstituted with 19 ml of sterile dH₂O, creating 20 ml of a 10,000-μg/ml solution. To create the peak-level stock solution, 1 ml of the 10,000-μg/ml VOR solution was added to 20.3 ml of sterile dH₂O, creating 21.3 ml of a 470-μg/ml stock solution. A 0.1-ml aliquot of this peak-level VOR stock solution contained 47 μg of VOR, corresponding to the amount of drug present in 10 ml of blood. For preparation of the trough-level VOR stock solution, 0.5 ml of the 10,000-μg/ml VOR solution was added to 15.8 ml of sterile dH₂O, creating 16.3 ml of a 306-μg solution. An aliquot of 0.1 ml of this trough-level stock solution contained 30.6 μg of VOR, corresponding to the amount of drug present in 10 ml of blood.

For preparation of the caspofungin stock solution, Cancidas vials containing 50 mg of standard laboratory powder were purchased from Merck, Inc., and reconstituted with 10.8 ml of sterile dH₂O per vial, resulting in 10.8 ml of a 5,056-μg/ml stock solution of caspofungin. Peak-level stock solution was prepared by adding 3 ml of the stock solution to 16 ml of sterile dH₂O, resulting in 19 ml of a 800-μg/ml stock. A 0.1-ml aliquot of this solution contained 80 μg of CAS, equivalent to the amount found in 10 ml of blood. For preparation of the trough-level stock solution, 0.5 ml of dH₂O was added to 15.3 ml of the initial CAS stock solution, creating 15.8 ml of a 160-μg/ml trough-level stock solution. A total of 0.1 ml of this stock contained 16 μg CAS, equivalent to the amount present in 10 ml of blood.

BC bottle inoculation/incubation. Suspensions of the test strains of *Candida* isolates were prepared in sterile 0.85% saline (NS) to achieve a 0.5 McFarland suspension of the organism. Through serial 1:100 dilutions using 5-ml NS blanks an approximate final inoculum concentration of 10 to 100 CFU/ml was achieved. The final inoculum size was verified by plating 0.1 ml of the suspension on a Sabouraud dextrose agar plate.

Using an aseptic technique, Bactec Plus Aerobic/F blood culture bottles (Bactec FX) and aerobic VersaTREK Redox 1 (80 ml, with stir bar) were each filled with 10 ml of recently donated (<5 days prior to use in this study), human whole blood (Interstate Blood Bank, Inc., Memphis, TN). The blood from healthy donors was collected into 500-ml bags, using sodium polyanethanesulfonate (SPS) as an anticoagulant. For each observation, the above-referenced antifungal agents were tested against specific *Candida* isolates, and for each observation the testing was performed in triplicate. All BC bottles for each CMBCS were inoculated with 0.1 ml of the final suspension of the *Candida* isolates. Serving as positive controls, three BC bottles for each observation and BC system received 0.1 ml sterile 0.85% saline in addition to the 10 ml human blood and 0.1-ml suspension of a *Candida* sp. In addition to human blood and the *Candida* suspension outlined above, three BC bottles for each observation/BC system were inoculated with 0.1 ml of the antifungal agent at the peak concentration, and three BC bottles were inoculated with 0.1 ml antifungal agent at the trough concentration. Lastly, one BC bottle per observation and BC system was inoculated with 0.2 ml of 0.85% sterile saline; serving as negative controls, these BC bottles did not receive either aliquots of *Candida* suspension or antifungal agent. After inoculation with respective aliquots of human blood, *Candida* isolate suspension, antifungal agents at either the peak or trough concentration, and/or

saline, all BC bottles were gently inverted for mixing and then immediately placed into the corresponding CMBCS. All bottles were incubated at 35°C with continuous agitation in their respective CMBCS for a standard 5-day incubation cycle (5).

When BC bottles were flagged as positive by the CMBCS, the length of time to detection (LTD) was documented. Growth within positive BC bottles was verified by Gram stain, culture on Sabouraud dextrose agar, and subsequent organism identification by the API20C method (bioMérieux).

Terminal subcultures were performed on all BC bottles that were negative (no growth) at 5 days, and an aliquot of 0.1 ml from each BC bottle was subcultured onto Sabouraud dextrose agar and incubated at 35°C for 3 days.

Statistics. The ability of each CMBCS to recover the organism (growth/no growth) was evaluated using the Fisher exact or chi-square test. Blood culture bottles were defined as negative after 120 h (5 days) of incubation without CMBCS detecting growth. The LTD (in hours) for positive blood cultures was analyzed using the Wilcoxon rank-sum (Mann-Whitney) test. Statistical analyses, including measures of association, descriptive statistics, and survival analysis (Kaplan-Meier survival method), were performed using Stata 9.2 (Stata Corporation, TX).

RESULTS

A total of 721 seeded blood culture bottles were incubated in each of the CMBCS (VersaTREK system and the Bactec FX system) to evaluate their ability to detect *Candida* spp. in BC bottles with and without the presence of select antifungal agents at therapeutic drug levels. Both CMBCS were consistently unable to detect the growth of organisms in BC bottles seeded with either *C. krusei* (1 isolate), *Cryptococcus laurentii* (1 isolate), or *Cryptococcus neoformans* (3 isolates). The terminal subcultures performed from BC bottles for these 5 organisms were negative. The results for these organisms (45 BC bottles per CMBCS) were not included in the statistical analysis. We also excluded data for all negative-control BC bottles, as they were included only to serve as markers for adherence to the aseptic technique throughout the study and, as expected, they did not flag positive for growth.

With the exception of *C. glabrata*, which tested as susceptible-dose dependent against fluconazole, *Candida* spp. used in this study were susceptible to all antifungal agents tested (Table 1).

As shown in Table 2, of the 226 seeded positive-control BC bottles (no antifungal agent present) in the Bactec FX system, 220 were positive for the growth of *Candida* spp. (recovery, 97.4%); 224/226 corresponding BC bottles in the VersaTREK system were positive for growth (recovery, 99.1%). There was no statistically significant difference in the abilities of the two CMBCS to detect growth of *Candida* in BC bottles without the presence of antifungal agents ($P = 0.154$) (Table 2). However, *C. glabrata* recovery with VersaTREK (97.2%) was better than that for Bactec FX (86.1%), albeit not statistically significant ($P = 0.088$). The inability of the Bactec Plus Aerobic/F medium to detect growth and/or the delayed detection of growth for *C. glabrata* has been described previously (15). Using the Lytic/10 Anaerobic/F BC bottles with the Bactec 9240, Foster et al. demonstrated the need for the anaerobic blood culture bottle to improve the recovery of *C. glabrata* (11). In addition, differences in BC broth composition, which is at least in part proprietary information to the respective manufacturer, may account for differences in the ability to recover *C. glabrata* in the two CMBCS studied here. At least one other study suggested that *C. glabrata* has an apparent predilection for certain components of BC broths, in particular for components present in the BD lytic anaerobic and Plus anaerobic media (11).

TABLE 2. Recovery of isolates from CMBCS stratified by *Candida* spp.

Yeast	Instrument	Positive control			Any antimicrobial			Peak-concentration antimicrobial			Trough-concentration antimicrobial		
		No. of isolates with growth (%)	No. of isolates with no growth	<i>P</i> value	No. of isolates with growth (%)	No. of isolates with no growth	<i>P</i> value	No. of isolates with growth (%)	No. of isolates with no growth	<i>P</i> value	No. of isolates with growth (%)	No. of isolates with no growth	<i>P</i> value
All organisms	Bactec FX	220 (97.4)	6	0.154	374 (83.1)	76	<0.001	176 (78.6)	48	<0.001	198 (87.6)	28	<0.001
	VersaTREK	224 (99.1)	2		228 (50.7)	222		100 (44.6)	124		128 (56.6)	98	
<i>C. albicans</i>	Bactec FX	120 (100)	0	0.316	209 (87.5)	30	<0.001	98 (82.4)	21	<0.001	111 (92.5)	9	<0.001
	VersaTREK	119 (99.6)	1		96 (40.2)	143		39 (32.8)	80		57 (47.5)	63	
<i>C. glabrata</i>	Bactec FX	31 (86.1)	5	0.088	43 (59.7)	29	0.298	17 (47.2)	19	0.237	26 (72.2)	10	0.789
	VersaTREK	35 (97.2)	1		49 (68.1)	23		22 (61.1)	14		27 (75.0)	9	
<i>C. parapsilosis</i>	Bactec FX	22 (95.7)	1	0.312	47 (100)	0	<0.001	23 (100)	0	<0.001	24 (100)	0	<0.001
	VersaTREK	23 (100)	0		20 (42.6)	27		6 (26.1)	17		14 (58.3)	10	
<i>C. tropicalis</i>	Bactec FX	47 (100)	0	NA	75 (81.5)	17	0.41	38 (82.6)	8	0.214	37 (80.3)	9	0.101
	VersaTREK	47 (100)	0		63 (68.5)	29		33 (71.7)	13		30 (65.2)	16	

TABLE 3. LTD for *Candida* spp.^a

Yeast	Instrument	Positive control				Any antimicrobial			
		% Growth	Mean h (median)	CI	P value	% Growth	Mean h (median)	CI	P value
All organisms	Bactec FX	97.4	31.67 (28.57)	(29.62–33.73)	<0.001	83.1	37.34 (31.07)	(35.28–39.40)	<0.001
	VersaTREK	99.1	26.04 (26.36)	(25.40–26.68)		50.7	48.12 (42.81)	(45.28–50.95)	
<i>C. albicans</i>	Bactec FX	100	28.66 (28.19)	(27.86–29.46)	0.008	87.5	36.71 (30.64)	(34.01–39.40)	<0.001
	VersaTREK	99.2	27.44 (26.85)	(26.86–28.02)		40.2	48.83 (39.03)	(44.13–53.54)	
<i>C. glabrata</i>	Bactec FX	86.1	60.91 (51.80)	(52.66–69.16)	<0.001	59.7	67.04 (62.92)	(61.34–72.74)	<0.001
	VersaTREK	97.2	23.97 (23.22)	(22.54–25.40)		68.1	42.23 (38.80)	(36.91–47.54)	
<i>C. parapsilosis</i>	Bactec FX	95.7	33.15 (33.13)	(32.31–33.98)	0.617	100	35.22 (34.96)	(34.02–36.43)	<0.001
	VersaTREK	100	33.27 (33.35)	(32.38–34.17)		42.6	48.94 (42.16)	(42.02–55.86)	
<i>C. tropicalis</i>	Bactec FX	100	19.40 (19.30)	(18.90–19.89)	0.021	81.5	23.39 (21.27)	(21.77–25.01)	<0.001
	VersaTREK	100	20.51 (20.46)	(19.69–21.33)		68.5	51.34 (46.95)	(45.56–57.12)	

^a CI, confidence interval.

A combined total of 450 BC bottles containing an antifungal agent at either the peak or trough concentration were used for each CMBCS. With Bactec FX, 374/450 (83.1%) BC bottles were positive for growth of *Candida*, whereas for VersaTREK only 228/450 (50.7%) BC bottles were positive for the growth of *Candida*. The recovery of *Candida* spp. at the peak levels of antifungal agents was 78.6% for Bactec FX and 44.6% for VersaTREK. At the trough-level concentrations, overall recovery for Bactec FX was 87.6% and 56.6% for VersaTREK. In the presence of the commonly used antifungal agents tested in this study, regardless of peak- or trough-level concentrations, the ability to recover *Candida* spp. in the Bactec FX system was significantly better than that of the VersaTREK system ($P < 0.001$). Detailed data, stratified by the type of *Candida* sp., are displayed in Table 2.

Details of recovery and length of time to detection for each

CMBCS, stratified by CMBCS and *Candida* sp., are shown in Table 3. For the seeded BC bottles (all organisms) within the positive-control group (no antifungal agent), the median LTD for the VersaTREK system was 2.2 h faster than Bactec FX ($P < 0.001$). The LTD for the bottles containing antifungal agents in Bactec FX was significantly shorter than the LTD with VersaTREK ($P < 0.001$) (Table 3) for all organisms, except for *C. glabrata*. Differences in LTD for organism recovery between both CMBCS varied by *Candida* sp. Because the recovery of organisms at peak- and trough-level concentrations did not differ significantly, we combined both sets of data for the LTD analysis. To visualize the time to detection of both systems using seeded BC bottles, the cumulative proportion of positive bottles by time was plotted graphically (Fig. 1) and estimated by a survival analysis. In the absence of an antifungal agent and as expected from a previous LTD analysis, a

FIG. 1. Kaplan-Meier time-dependent analysis of the proportion (y axis) of positive blood culture bottles in the absence and presence of antifungal agent.

greater proportion of organisms were recovered sooner by the VersaTREK system ($P < 0.001$). In the presence of antifungal agents, however, Bactec FX was consistently better than VersaTREK ($P < 0.001$), as demonstrated in Table 3 and visualized in Fig. 1. The exception to this observation was the recovery for *C. glabrata*, for which the VersaTREK system performed slightly better than the Bactec FX system (Table 3).

DISCUSSION

Several published studies compared the performances of the currently available CMBCS (10, 14–16, 27, 28), comparing foremost the Bactec 9240 and the BacT/Alert systems. Only one study compared the performance of the VersaTREK system to the BacT/Alert blood culture system (20). The majority of these studies investigated the ability and/or LTD to detect bacterial organisms, with only a few studies including data on the systems' performances in the recovery of yeast. Except for one study focused on the recovery of different *Candida* spp. (14), most studies focused foremost on *Candida albicans*.

To our knowledge, our study is unique in comparing the performances of CMBCS for their ability to detect the growth of *Candida* spp. in seeded blood cultures supplemented with and without therapeutic levels of commonly used antifungal agents. George et al. demonstrated that the recovery and length of time to detection differed with regard to inoculum size in seeded BCs (13). To eliminate bias, we chose the model of a simulated seeded blood culture study and standardized the inoculated blood volume, test organisms, and antifungal agent, using the same total inoculum for both CMBCS. Further, blood culture bottles were inoculated in an alternating fashion between observations to eliminate systematic error.

The Bactec and VersaTREK systems differ significantly in design and operation. The Bactec FX system uses an internal fluorometric sensor for the detection of CO₂ production by the microorganisms. The VersaTREK system, by the use of an external pressure sensor, detects pressure changes in the bottle headspace as a result of production and consumption of gas by the growing microorganisms. The two systems also differ in their established time intervals for sensor readings, composition of the blood culture medium, the type and composition of the anticoagulant, and the volume of broth within the BC bottles. Furthermore, the VersaTREK Redox 1 aerobic bottles used in this study contain a stir bar that creates a vortex within the BC bottle. The Bactec Plus Aerobic/F bottles contain resins to absorb antimicrobials present in the blood.

We found that both CMBCS in the absence of antifungal agents demonstrated no difference in overall recovery of *Candida* spp. ($P = 0.154$). Most clinical laboratories using CMBCS utilize a routine 5-day incubation cycle for blood culture bottles. Most bacterial isolates are well isolated within this time frame; however, debate continues over the need for extended incubation of BCs for recovery of yeast (5, 14, 15). While the two CMBCS used in our study differ significantly in their respective designs to detect growth of organisms, we observed somewhat equal abilities to detect organism growth in the absence of antifungal agents. The observed differences in LTD may be related to the differences in detection method and/or the BC broth used for the respective system. These data support findings reported by other investigators that most epi-

sodes of candidemia may be diagnosed within the first 48 h of BC bottle incubation, with the exception of the recovery of *C. glabrata* (13, 16).

Results differed significantly between the two systems in the presence of antifungal agents. The VersaTREK system demonstrated poor performance in the recovery of *Candida* spp. in the presence of any type of antifungal agent, regardless of trough- or peak-level concentration. These observations are particularly important when considering the changing epidemiology of bloodstream infections for both community-acquired and hospital-acquired BSI and recent changes in the approach to treatment and prophylaxis. Improvements in diagnostic methods and implementation of prophylactic treatment of high-risk patients have been shown to reduce invasive candidiasis by as much as 50% and significantly improve clinical outcomes (6, 24, 32). In two recently published studies delay in treatment of candidemia was associated with increased mortality during hospitalization (12, 21). Despite the overall scarcity of data-driven evidence, the use of empirical antifungal therapy is a commonly accepted practice (24). While selection of empirical treatment is often problematic because of emerging drug resistance and cost constraints for health care institutions, recent studies found excellent *in vitro* susceptibilities to newer triazole drugs for a large collection of *Candida* spp. (8, 23). Fluconazole and echinocandins are currently the most commonly used antifungal agents for the empirical treatment of candidemia.

All of the *Candida* isolates used in our study tested susceptible to the antifungal agents used for BC bottle inoculation procedures. The difference between the CMBCS in their respective abilities to recover *Candida* spp. is most likely attributed to the differences in the BC media as described above. The Bactec Plus Aerobic/F medium contains resins designed for the adsorption/inactivation of antimicrobial agents; the VersaTREK Redox 1 medium contains 80 ml of a proprietary broth mixture without such resins. Our data suggest that a simple dilution effect resulting from the mixture of 10 ml blood containing antifungal agents and 80 ml of broth may not be sufficient to effectively reduce the antifungal effect to allow sufficient organism growth. Considering this fact together with the difference in recovery by the two CMBCS studied here, the commonly accepted clinical practice of empirical and/or prophylactic antifungal therapy may have an impact on the ability of microbiology laboratories to recover yeast from blood cultures obtained from such patients. The results of this study clearly illustrate significant differences in the ability and performance of two CMBCS to recover *Candida* spp. from seeded BCs supplemented with antifungal agents, intended to simulate BCs from patients who received antifungal therapy at the time when BCs were obtained.

A limitation of this study is the small number of isolates tested for some of the *Candida* spp. All of the *Candida* isolates tested susceptible at fairly low MICs, and we did not investigate the performance of the two CMBCS with organisms at higher MICs or organisms with resistance to any antifungal agent. Further, our study may have had a selection bias with regard to the *Candida* isolates chosen for testing, as all clinical isolates used in the study were previously isolated by our clinical laboratory's CMBCS, using the VersaTREK system. Lastly, we recognize that in the present study design, the per-

formance comparison for both CMBCS was done using aerobic blood culture media alone. The apparent predilection of *C. glabrata* for anaerobic growth conditions and specific components of BC broths will require additional studies comparing the CMBCS utilizing anaerobic BC bottles.

In conclusion, the Bactec FX system using the Bactec Plus Aerobic/F blood culture medium and the VersaTREK system using the Redox 1 aerobic blood culture medium had comparable abilities to recover various *Candida* spp. from seeded blood cultures in the absence of an antifungal agent, with the exception of *C. glabrata*. In the absence of antifungal agents, the VersaTREK had a statistically significantly shorter LTD than the Bactec FX. However, in the presence of therapeutic levels of commonly used antifungal agents, the Bactec FX system demonstrated a significantly greater recovery of organisms as well as a shorter LTD for various *Candida* spp. This observation may be particularly important, considering the common and increasing use of empirical antifungal therapy. Further studies are necessary to investigate the performance of other commercially available CMBCS as well as *Candida* sp. and BC medium formulations not tested in this study.

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