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Comparison of Du Pont Isolator and Roche Septi-Chek for Detection of Fungemia

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The rapid detection of fungemia in hospitalized patients is imperative, particularly for those who are immunocompromised. Our laboratory compared the Roche Septi-Chek with the Du Pont Isolator for the recovery of fungi from blood. Of 23,586 matched pairs of blood cultures, 199 were positive. The Isolator detected 178 (89.4%) and the Septi-Chek detected 119 (59.7%) of all positive isolates. The mean recovery time for the Isolator and Septi-Chek was 2.2 and 4.9 days, respectively. The Isolator detected fungemia earlier than the Septi-Chek did and was the only culture system positive in 83% of 53 patients, whereas the Septi-Chek system yielded the same results in only 13% of the patients. The Isolator provides a more rapid and sensitive method for the recovery of fungi from blood.

Fungemia has become an important problem in hospitalized patients because of an increasing population of immunocompromised hosts and because of the frequent use of invasive diagnostic, as well as therapeutic, modalities. The diagnosis of opportunistic fungal infections continues to be a challenge for clinicians and microbiologists. The recovery of fungi from blood is an important tool for the diagnosis of certain systemic fungal infections, including those caused by *Candida* species, *Cryptococcus neoformans*, and *Histoplasma capsulatum*. Several improvements in blood culture techniques have been developed and evaluated during the past 10 years. The use of vented blood culture bottles enhanced the recovery of *Candida* species and *Cryptococcus neoformans*, in contrast to the conventional unvented bottle (4–7). In 1975, Roberts and Washington (8) described the use of a biphasic vented system (brain heart infusion [BHI] broth and agar slant) which significantly improved the recovery rate of fungi from blood. This system increased the recovery rate of *Candida* species and *Cryptococcus neoformans* when compared with a vented conventional blood culture bottle containing tryptic soy broth (2). Isolates of *Candida albicans*, *Candida tropicalis*, and *Candida parapsilosis* were detected in an average of 4.2 (vented biphasic bottle) versus 7.1 days (conventional bacterial blood culture bottle) (2).

The introduction of a commercial biphasic system, the Roche Septi-Chek (RSC) blood culture bottle with its attached agar slide chamber, and the more recently introduced lysis-centrifugation blood culture system, the Isolator (E. I. du Pont de Nemours & Co., Inc.), offered us the opportunity to compare both techniques for the detection of fungemia. The latter system utilizes a tube that contains components which lyse leukocytes and erythrocytes. Once removed from the intracellular environment, the microorganisms are concentrated by centrifugation and the concentrate is inoculated onto appropriate culture media. The Isolator system, which has been previously evaluated (3), recovered 90.3% of the positive cultures compared with 63.6% detected by the BHI biphasic bottle. The mean recovery time for yeasts was 2.1 days by the Isolator and 4.9 days by the BHI biphasic bottle.

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The present study was undertaken to compare, in a retrospective fashion, the RSC system with the Isolator system for the detection of fungemia.

MATERIALS AND METHODS

Blood culture data collected during an 11-month period were reviewed in a retrospective fashion. Blood samples (20 ml) from patients suspected of having fungemia were collected, and 10 ml of each sample was inoculated into an RSC bottle and the other 10 ml was inoculated into an Isolator tube (matched pairs).

The RSC bottles (containing 70 ml of tryptic soy broth with 0.05% sodium polyanetholesulfonate) were transiently vented upon arrival in the laboratory. The RSC slide chamber, containing chocolate, MacConkey, and malt agars, was attached to the bottle at this time, and the bottle was tipped to inoculate all agar surfaces with the blood-broth mixture. All bottles were incubated at 35°C and examined macroscopically twice on day 1, daily for the next 6 days, and once on day 14 before they were discarded. Agar surfaces were examined at the time of each macroscopic examination, and they were reinoculated with the blood-broth mixture at this time.

After Isolator tubes were inoculated, blood was mixed with the chemical components by inverting each tube several times. The tube was centrifuged for 30 min at 3,000 × *g*, and equal amounts of its sediment were inoculated onto the surface of agar plates containing chocolate agar, sheep blood agar, inhibitory mold agar, BHI agar, and Sabouraud 2% dextrose agar. Cultures were incubated for 30 days at 30°C and examined daily for the first 14 days, followed by weekly observations for the remainder of the incubation period. All fungi recovered during the study were identified by previously published methods (9). The microbiological data were analyzed to determine whether significant differences in the recovery rate were present in the RSC and the Isolator system and to ascertain which system provided positive culture results earlier. For comparison of both systems when two different fungal species were recovered from the same blood culture, each isolate was considered to be two different blood cultures.

TABLE 1. Detection of fungi in blood cultures

Organism(s)	No. of isolates	No. (%) of fungi recovered by:				
		Isolator	Isolator only	Septi-Chek	Septi-Chek only	Both systems
Candida albicans	98	88 (90)	44 (45)	54 (55)	10 (10)	44 (45)
Candida tropicalis	46	39 (85)	10 (22)	36 (78)	7 (15)	29 (63)
Candida glabrata	28	25 (89)	13 (46)	15 (54)	3 (11)	12 (43)
Candida parapsilosis	10	9 (90)	3 (30)	7 (70)	1 (10)	6 (60)
Candida guilliermondii	2	2	0	2	0	2
Candida zeylanoides	1	1	0	1	0	1
Cryptococcus neoformans	8	8 (100)	5 (62.5)	3 (37.5)	0	3 (37.5)
Histoplasma capsulatum	4	4	4	0	0	0
Trichosporon beigelii	1	1	0	1	0	1
Beauveria species	1	1	1 (100)	0	0	0
Total	199	178 (89.4)	80 (40.2)	119 (59.7)	21 (10.5)	98 (49.2)

To evaluate the clinical significance of each episode of fungemia, the following parameters were considered: number of positive blood cultures, recovery of the same organism from sites other than blood, and presence of fever, chills, or hypotension (9). Also, fungemia was considered to be clinically significant if it was documented from at least two separate blood cultures.

RESULTS

Over the 11-month period of the study, 23,586 matched pairs of fungal blood cultures were performed and 199 (0.84%) were positive, representing a total of 53 patients. The most commonly recovered organisms were, in order of frequency, *Candida albicans*, *Candida tropicalis*, and *Candida glabrata*. Overall, the Isolator recovered 178 (89.4%) of the isolates, whereas the RSC recovered 119 (59.7%) ($P < 0.001$). Compared with the RSC, the Isolator increased the detection rate by 30% (59 of 199). The Isolator detected 90% of the *Candida albicans* and 89% of the *Candida glabrata* isolates, whereas the RSC detected 55 and 54%, respectively. Eight blood cultures were positive for *Cryptococcus neoformans*, all of which were detected by the Isolator, whereas only three were detected by RSC. *Histoplasma capsulatum* was recovered from four blood cultures, all of which were detected only by the Isolator (Table 1). Of the 199 positive blood cultures, 40.2% were detected only by the Isolator and 10.5% were detected only by the RSC, whereas 49.2% were detected by both systems.

TABLE 2. Recovery times of fungi by the Isolator and Septi-Chek

Organism(s)	Time (days) to detection[a]			
	Isolator		Septi-Chek	
	Mean	Range	Mean	Range
Candida albicans	2	1–5	4.8	2–14
Candida tropicalis	1.7	1–3	3.3	1–15
Candida glabrata	1.7	2–7	5.6	3–13
Candida parapsilosis	1.7	1–2	4.2	2–14
Candida guilliermondii	1.5	1–2	7	1–13
Candida zeylanoides	2	2	3	3
Cryptococcus neoformans	2.3	2–3	7	5–11
Histoplasma capsulatum	13	12–14		
Trichosporon beigelii	2	2	9	9
Beauveria species				

[a] The mean recovery time for these species was 2.2 days by the Isolator and 4.9 days by Septi-Chek.

The mean recovery time for all isolates (Table 2) was 2.2 days for the Isolator and 4.9 days for the RSC. The mean recovery time for *Candida albicans*, *Candida tropicalis*, and *Candida glabrata* was 2, 1.7, and 3 days, respectively, for the Isolator versus 4.8, 3.3, and 4.6 days, respectively, for the RSC.

There were patients in whom fungemia was detected first or only by one of the two systems (Table 3). The Isolator was the first or only system to detect fungemia in 44 patients (83%), whereas the RSC detected fungemia in only 7 patients (13%). Fungemia was considered clinically significant in 49 patients, with 43 (87.7%) detected first or only by the Isolator. Of the four patients in whom fungemia was deemed clinically insignificant, three were detected first or only by the RSC and one was detected by the Isolator.

DISCUSSION

This retrospective evaluation of two different blood culture systems for the recovery of yeasts and filamentous fungi demonstrated that the Isolator system detected 89.4% of the positive cultures and the RSC detected only 59.7%. At the same time, the recovery time for all fungi was markedly reduced by the Isolator system, as compared with the RSC. All *Candida* species were recovered in 3 days or less by the Isolator.

The Isolator either detected fungemia earlier than the RSC system did or was the only blood culture system that recovered fungi in 83% of the patients, with only one case of fungemia considered clinically insignificant. In contrast, the RSC was the first or only system to detect fungemia in seven patients (13%), with three of the cases of fungemia considered clinically insignificant (1).

It is interesting to note that two different species of *Candida* were recovered from seven patients. Of the 14 different isolates, 13 (92.8%) were detected only or earlier by

TABLE 3. Clinical significance of earlier or only detection by one system[a]

Clinical significance of fungemia	No. of patients with fungemia detected by:			
	Isolator		Septi-Chek	
	Only	Earlier	Only	Earlier
Significant	14	29	3	1
Nonsignificant	1		3	

[a] Fungemia was detected the same day by both systems in two patients.

the Isolator, and only one isolate was recovered the same day by both systems.

The improved blood culture methods for the diagnosis of fungemia, primarily the use of vented blood culture bottles and the use of biphasic media, have been further enhanced by the introduction of the Isolator system. The results of this present study are similar to our previous comparison of the BHI bottle versus the Isolator in regard to recovery and detection times (3). In conclusion, when compared with the RSC, the Isolator system provides a more rapid, sensitive technique for the recovery of yeasts and filamentous fungi from blood and is the preferred method.

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