JOURNAL OF CLINICAL MICROBIOLOGY, Sept. 1990, p. 1925–1927
0095-1137/90/091925-03$02.00/0

Vol. 28, No. 9

Clinical Comparison of Isolator and BACTEC 660 Resin Media for Blood Culture

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Received 2 March 1990/Accepted 11 June 1990

The 10-ml Isolator system (E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.) was compared with the BACTEC 16A-17A nonradiometric resin system (Johnston Laboratories, Inc., Towson, Md.) for isolation of organisms from 6,839 paired blood cultures. Equal volumes of blood (6 to 10 ml for each Isolator and 3 to 5 ml for each BACTEC bottle) were cultured in parallel in the two systems, and 600 isolates that were judged to be clinically significant by chart review were recovered during the study. The BACTEC resin system detected 510 (85%) and the Isolator system detected 435 (72%) of the clinically significant isolates ($P < 0.001$). Of 45 polymicrobial blood cultures, the BACTEC system detected 32 (71%) and the Isolator system detected 21 (47%) ($P < 0.05$). Of 253 gram-negative bacilli isolated during the study, 30% were detected only in the BACTEC system and 16% were detected only in the Isolator system ($P < 0.001$), and of 56 nonfermentative or fastidious gram-negative bacilli detected, 46% were recovered only in the BACTEC system, while 14% were detected only in the Isolator system ($P < 0.001$). Of 86 streptococci isolated during the study, 30% were detected only in the BACTEC system, and 4% were detected only in the Isolator system ($P < 0.001$). Recoveries of anaerobic bacteria, staphylococci, and yeasts were equivalent in the two systems. Organisms judged to be contaminants were detected in approximately 1% of the cultures in each system. The results suggest that use of resin media renders the BACTEC nonradiometric system equivalent or superior to the Isolator system for detection of clinically significant organisms in blood cultures.

Several previous studies have suggested that the Isolator system (E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.) is superior to broth culture systems for detection of bacteremia and fungemia (5). Studies comparing the Isolator system with BACTEC radiometric nonresin broth media (BACTEC system; Johnston Laboratories, Inc., Towson, Md.) have demonstrated the detection of 15 to 18% more clinically significant organisms by the Isolator system (4). Factors that may contribute to the superior performance of the Isolator system in previous studies include the lysis of phagocytic cells, removal of organisms from natural inhibitory factors in human blood, and removal of organisms from antibiotics that may have been administered to the patient. The addition of resins to broth culture media aids the removal of antibiotics and other inhibitory substances from the blood samples, and previous studies have demonstrated improved recovery of clinically significant organisms from such media compared with those recovered from standard media (2, 3). A recent study comparing the Isolator system with BacTec radiometric resin media demonstrated that the two systems are equivalent in their performances (1). The purpose of the present study was to compare the detection of bacteremia and fungemia by the Isolator system and the BACTEC system with nonradiometric resin media in a parallel, volume-matched evaluation.

MATERIALS AND METHODS

Blood samples for culture were collected by the phlebotomy team or house staff by using a kit that contained a 10-ml Isolator tube (E. I. duPont de Nemours and Co., Inc.), bottles of aerobic (16A) and anaerobic (17A) nonradiometric BACTEC resin media (Johnston Laboratories), needles, and disinfectants needed for the venipuncture. The venipuncture site was cleansed with alcohol and disinfected by application of povidone iodine for at least 30 s. The blood sample was divided equally between the Isolator and the BACTEC bottles. The minimum volumes acceptable for entry into the study were 6 ml for the Isolator system and 3 ml per BACTEC bottle. The volume of blood in the Isolator tubes was determined by comparing each patient specimen with a series of Isolator tubes containing 5, 6, 7, 8, 9, or 10 ml of water. Similarly, the BACTEC clinical specimens were compared with a series of bottles containing 3, 4, or 5 ml of water.

The Isolator tubes were processed in the laboratory according to the instructions of the manufacturer; and the concentrate was divided between two aerobic 5% sheep blood agar plates, a chocolate agar plate, and an anaerobic brucella agar plate (Prepared Media Laboratories, Tualatin, Oreg.). The sheep blood agar and the chocolate agar plates were incubated in 5% CO_2 in air. The brucella agar plates were incubated under anaerobic conditions in GasPak jars (BBL Microbiology Systems, Cockeysville, Md.). The plates were inspected daily for 4 days. The BACTEC bottles were incubated and analyzed on the BACTEC 660 nonradiometric system according to the recommendation of the manufacturer. Readings were taken on the aerobic bottles twice daily for the first 2 days and then daily up to day 7. Readings were taken on the anaerobic bottles daily for 7 days. Terminal blind subcultures were performed on day 7.

Charts were reviewed by two of us (F.J.R. and I.G.) to determine the clinical significance of positive blood cultures. The information used to assess clinical significance included fever, hypotension, administration of antibiotics in association with the positive blood culture, isolation of the same organism from another infected site, the organism species,

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TABLE 1. Comparative detection of gram-negative bacilli by nonradiometric BACTEC resin media and the Isolator system

Organism	Total	No. detected by:		P
		BACTEC	Isolator	
Acinetobacter spp.	6	3	5	NS[a]
Actinobacillus spp.	4	4	0	0.01
Bacteroides spp.	4	4	3	NS
Campylobacter spp.	3	3	0	0.05
Citrobacter spp.	6	4	5	NS
Enterobacter spp.	15	12	11	NS
Escherichia spp.	128	109	95	<0.05
Klebsiella spp.	26	22	18	NS
Proteus spp.	17	14	15	NS
Pseudomonas spp.	25	20	15	NS
Salmonella spp.	5	4	4	NS
Other[b]	14	14	7	<0.001
Total	253	213	178	<0.001

[a] NS, Not significant.

[b] CDC group VE2 (n = 1), *Hafnia alvei* (n = 2), *Haemophilus influenzae* (n = 2), *Neisseria* sp. (n = 1), *Providencia stuartii* (n = 2), *Alcaligenes faecalis* (n = 1), *Morganella morganii* (n = 2), *Serratia marcescens* (n = 2), and mixed anaerobic bacteria (n = 1).

TABLE 2. Comparative detection of gram-positive bacteria and yeasts by nonradiometric BACTEC resin media and the Isolator system

Organism	Total	No. detected by:		P
		BACTEC	Isolator	
Candida spp.	30	20	21	NS[a]
Cryptococcus spp.	2	1	1	NS
Clostridium spp.	4	2	2	NS
Enterococcus spp.	26	24	17	<0.05
Listeria spp.	12	12	10	NS
Staphylococcus aureus	140	121	111	NS
Coagulase-negative staphylococci	44	33	30	NS
Streptococcus pneumoniae	38	37	27	<0.005
Viridans group streptococci	22	22	16	<0.05
Other[b]	29	25	21	NS
Total	347	297	256	<0.001

[a] NS, Not significant.

[b] *Aerococcus* sp. (n = 1); diphtheroids (n = 2); *Peptococcus* spp. (n = 2); and group A (n = 1), group B (n = 9), group C (n = 7), and group G (n = 6) and nonhemolytic streptococci (n = 1).

number of positive cultures, and the time required for the culture to become positive.

Statistical analyses comparing the Isolator system results with the BACTEC system results were done by chi-square analysis and the Fisher exact test by using Analyst software (Epic Systems Corp., Madison, Wis.).

RESULTS

A total of 6,839 blood cultures were analyzed in parallel by the Isolator and BACTEC resin media, and 600 clinically significant isolates were recovered from these cultures. Of these clinically significant isolates, 510 (85%) were detected by the BACTEC system and 435 (72%) were detected by the Isolator system ($P < 0.001$). Twenty-eight percent of the clinically significant isolates were detected only by the BACTEC resin system, and 15% were detected only by the Isolator system ($P < 0.001$). The specimens positive only by the Isolator system often had low colony counts. The total number of colonies detected from all Isolator-positive specimens averaged 665, but an average of only 12 colonies was detected from specimens positive by the Isolator system only. Fourty-five polymicrobial cultures were detected during the study, and 71 and 47% of these were found in the BACTEC and Isolator systems, respectively ($P < 0.05$). Organisms judged to be contaminants were recovered from 70 (1%) of the BACTEC cultures and from 41 (0.06%) of the Isolator cultures (an additional 148 Isolator cultures had contaminants outside the area of inoculation, but these were considered to be laboratory contaminants).

During the study, 253 clinically significant gram-negative bacilli were recovered, including 213 detected in the BACTEC resin system and 178 detected in the Isolator system ($P < 0.001$) (Table 1). For individual species of gram-negative bacilli, statistically significant differences in recovery were demonstrated only for the *Escherichia coli*, *Actinobacillus* spp., and other, mostly fastidious, bacteria. However, the BACTEC system detected significantly more members of the family *Enterobacteriaceae* as a group than did the Isolator system (165 versus 148 of 197; $P < 0.001$).

A total of 347 gram-positive bacteria and yeasts were recovered during the study (Table 2). The Isolator and BACTEC resin systems gave essentially equivalent recoveries of yeasts, staphylococci, and gram-positive bacilli. However, significant differences were noted in the overall recoveries of streptococci by the BACTEC and Isolator systems (83 versus 60 of 86; $P < 0.001$); and the BACTEC system recovered significantly more *Enterococcus* spp., *Streptococcus pneumoniae*, and viridans group streptococci. The two systems also recovered equivalent numbers of gram-positive and gram-negative anaerobic bacteria. Of the 510 isolates, 6 (1%) detected in the BACTEC system were recovered only by the blind subcultures. These isolates included two *Pseudomonas* spp., one *Enterococcus* sp., one *Listeria* sp., one *Bacteroides* sp., and one *Candida* sp. Three of these organisms were also detected by the Isolator system.

DISCUSSION

The results of this study demonstrate that the nonradiometric BACTEC system with resin media for blood culture provides enhanced detection of clinically significant organisms. The resin media provided significant enhancement of detection of pathogens overall; and advantages for detection of gram-negative bacilli, streptococci, and polymicrobial infections were particularly noted. When compared with the Isolator system, 28% of the clinically significant organisms encountered in the study were detected only by the BACTEC resin system, and 30% of gram-negative bacilli and streptococci were detected only by the BACTEC system. These findings indicate that the use of resin media significantly improves the performance of the BACTEC system relative to that of the Isolator system, and the BACTEC resin media system was equivalent or superior to the Isolator system for the recovery of all organism groups encountered in the study.

Previous studies indicated that the Isolator system is superior to traditional broth systems for the detection of bacteremia. For example, previous studies by one of us (M.T.K.) indicated that 27% of clinically significant blood culture isolates were recovered only in the Isolator system when compared with a system comprised of two 100-ml bottles of broth (6). Kellogg et al. (4) compared the Isolator and the radiometric BACTEC systems by using nonresin media and found that the Isolator system detected 15 to 18%

more clinically significant organisms overall and 34 to 36% more members of the family *Enterobacteriaceae* (4). These and other studies (5) indicate that the Isolator system provides enhanced recovery of clinically significant organisms when compared with traditional broth systems as well as with the BACTEC radiometric nonresin media system.

Several factors may contribute to the superior performance of the Isolator system compared with broth culture systems. Lysis of blood cells, especially phagocytic cells, may increase the detection of organisms that would otherwise be sequestered in or damaged by the cells. Centrifugation to remove the organisms from natural inhibitory substances in the blood (e.g., the killing effect of human serum against certain gram-negative bacilli) and from antibiotics may increase the yield of organisms from the Isolator system compared with those from broth culture systems. Recent studies suggest that the latter mechanism may be important because media that contain resins to remove inhibitory substances yield more significant isolates than does broth media without resins (2).

Two recent studies suggested that resin-containing media may improve the yield of BACTEC blood cultures. The BACTEC radiometric system, which uses resin media, provided for the recovery of clinically significant organisms equivalent to those recovered by the Isolator (1), and resin media compared with nonresin media significantly improved the performance of the BACTEC nonradiometric system (2). The results of the present study confirm and extend these findings by testing a larger number of cultures in parallel in a volume-matched study comparing the Isolator system with the nonradiometric BACTEC system with resin media. Our findings indicate that the use of resin media significantly improves the performance of the BACTEC nonradiometric system compared with that of the Isolator system.

ACKNOWLEDGMENTS

This work was supported in part by Johnston Laboratories.
We thank Shiela Sinkie for excellent technical assistance.

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