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Clinical Comparison of the Isolator and BacT/Alert Aerobic Blood Culture Systems

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The performance characteristics of the Isolator (Wampole Laboratories, Cranbury, N.J.) and the BacT/Alert (Organon Teknika Corporation, Durham, N.C.) aerobic blood culture systems were compared for 6,009 blood culture sets obtained from patients with suspected bloodstream infections. The BacT/Alert aerobic bottle [BTA(O_2)] was continuously agitated while it was incubated in 5% CO_2 at 36°C; culture plates prepared from the Isolator tube [I(O_2)] were incubated in 5% CO_2 at 37°C. From 394 blood cultures, 416 clinically significant isolates of bacteria and yeasts were recovered. The overall yields for BTA(O_2) and I(O_2) were not significantly different (319 versus 336; $P = 0.20$). I(O_2) recovered significantly more staphylococcus ($P < 0.05$) and yeast isolates ($P < 0.01$). BTA(O_2) recovered significantly more aerobic and facultatively anaerobic gram-negative bacilli ($P < 0.05$). In blood culture sets which produced growth of the same organisms in both the BTA(O_2) and I(O_2) systems, the BTA(O_2) system detected growth sooner, but more rapid identification was possible with the I(O_2) system by virtue of earlier isolation of colonies on solid media.

The Isolator (Wampole Laboratories, Cranbury, N.J.) manual blood culture system uses lysis-centrifugation to enhance the recovery of microorganisms (1). The BacT/Alert (Organon Teknika Corporation, Durham, N.C.) system is a fully automated blood culture system which uses photometric detection of CO_2 production for identification of microbial growth (7).

Studies have demonstrated the comparable and, in most cases, superior performance of either of these blood culture systems for detecting aerobic and facultatively anaerobic microorganisms, compared with other manual and automated blood culture systems (1–5, 7). In an effort to determine whether the Isolator or BacT/Alert aerobic blood culture system offered quantitative or qualitative advantages over the other, a prospective evaluation of these two systems was conducted. The performance characteristics of both systems for 6,009 blood cultures obtained from patients with suspected bloodstream infections at Mayo Clinic Jacksonville were compared.

(This study was presented in part at the 93rd General Meeting of the American Society for Microbiology, Atlanta, Ga., 16 to 20 May 1993.)

MATERIALS AND METHODS

This study was conducted from 1 August 1992 to 31 July 1993 at St. Luke's Hospital, the in-patient facility for the Mayo Clinic Jacksonville health care system. Eight to 10 ml of blood was inoculated into an aerobic bottle of BacT/Alert [BTA(O_2)] and an Isolator tube [I(O_2)]. Cultures in which BTA(O_2) or I(O_2) did not contain a minimum of 8 milliliters of blood were excluded from this study. The sequence of inoculation of BTA(O_2) and I(O_2) was rotated by technologists on a weekly (7-day) basis.

BTA(O_2) was incubated for 7 days at 36°C with supplemental (5%) carbon dioxide, and it was continuously agitated. The Isolator concentrate was subcultured onto the following solid media and incubated as follows. Trypticase soy agars with 5% sheep blood and chocolate were each incubated for 4 days at 37°C with 5% CO_2 and examined twice on day 1 and daily on days 2 through 4. Sabouraud and brain heart infusion agars with 5% sheep blood, gentamicin, and chloramphenicol were incubated for 21 days at 30°C and examined daily on days 1 through 7 and weekly for days 8 through 21.

The medical charts of patients whose blood cultures produced growth of coagulase-negative staphylococci, diphtheroids, *Bacillus* spp., and *Propionibacterium* spp. were reviewed by an infectious disease physician (W.C.H.). The criteria used for inclusion of these isolates were a potential source for bloodstream infection and either clinical signs or suspicion of sepsis. On the basis of this review, cultures which had likely been contaminated during venipuncture or in the laboratory were excluded from analysis.

Statistical analyses of comparisons of microorganisms isolated from BTA(O_2) and I(O_2) were performed by using the sign test for matched sets. Statistical analyses comparing the median times for identification of growth and median times for recovery of isolated colonies were performed by using the Wilcoxon signed-rank test (6).

RESULTS

During the study period, 6,858 blood cultures were obtained; 6,009 of these cultures contained the volume of blood required for entry in this study. Microbial growth was produced by 495 cultures (8.2%), of which 101, or 1.7% of those entered, were excluded from further analysis because of suspected contamination. Of the 6,009 cultures entered, 394 (6.5%) yielded growth of 416 significant aerobic or facultatively anaerobic isolates. Four obligately anaerobic isolates were recovered by BTA(O_2) and excluded from analysis.

The organisms recovered by the BTA(O_2) and/or I(O_2) systems are shown in Table 1. There was no significant difference in the total number of organisms recovered by each bottle [BTA(O_2), 319; I(O_2), 336] ($P = 0.20$). I(O_2) recovered significantly more staphylococci ($P < 0.05$) and yeasts ($P < 0.01$), while as shown in Table 1, BTA(O_2) recovered significantly more aerobic gram-negative bacilli ($P < 0.05$).

In Table 2, the times for identification of growth and recovery of isolated colonies are provided for blood cultures producing growth in both the I(O_2) and BTA(O_2) systems. For

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TABLE 1. Comparison of BTA(O_2) and I(O_2)

Organism	No. of isolates detected by:			
	Either or both	Both	BTA(O_2) only	I(O_2) only
Aerobic and facultatively anaerobic gram-positive bacteria	198	113	33	52
Staphylococci	132	69	23	40[a]
S. aureus	60	34	8	18
Coagulase-negative *Staphylococcus* spp.	72	35	15	22
Streptococci	60	44	9	7
Viridans group *Streptococcus* spp.	21	14	6	1
Streptococcus pneumoniae	10	10	0	0
Beta-hemolytic *Streptococcus* spp.	11	10	1	0
Enterococcus spp.	17	10	1	6
Group D nonenterococcus *Streptococcus* spp.	1	0	1	0
Other gram-positive aerobic and facultatively anaerobic bacteria	6	0	1	5
Bacillus spp.	1	0	1	0
Corynebacterium spp.	5	0	0	5
Aerobic and facultatively anaerobic gram-negative bacteria	147	87	39[a]	21
Enterobacteriaceae	102	64	22	16
E. coli	58	42	9	7
K. pneumoniae	27	14	8	5
K. oxytoca	6	6	0	0
Enterobacter cloacae	5	1	2	2
Serratia marcescens	3	1	1	1
Proteus mirabilis	2	0	2	0
Proteus rettgeri	1	0	0	1
Nonenteric gram-negative bacilli	37	21	12	4
Moraxella spp.	1	0	1	0
P. aeruginosa	15	10	5	0
other *Pseudomonas* spp.	9	4	3	2
Stenotrophomonas maltophilia	8	4	2	2
Flavobacterium spp.	3	2	1	0
Acinetobacter spp.	1	1	0	0
Other gram-negative aerobic bacteria	8	2	6	1
Haemophilus influenzae	2	0	2	0
Neisseria spp.	1	0	1	0
Campylobacter jejuni	1	0	1	0
Vibrio vulnificus	2	2	0	0
other gram-negative bacilli	3	0	2	1
Yeast	71	39	8	24[a]
C. albicans	35	22	5	8
Candida krusei	9	8	1	0
C. parapsilosis	12	2	0	10[a]
Candida tropicalis	2	2	0	0
C. glabrata	9	5	2	2
Candida lusitaniae	1	0	0	1
other *Candida* spp.	1	0	0	1
Rhodotorula spp.	1	0	0	1
Cladosporium spp.	1	0	0	1
Total	416	239	80	97

[a] $P < 0.05$.

each group of organisms in Table 2, BTA(O_2) identified growth significantly sooner, with mean differences between BTA(O_2) and I(O_2) ranging between 1.1 and 7.7 h, respectively. However, I(O_2) produced isolated colonies significantly sooner, with mean differences between I(O_2) and BTA(O_2) ranging from 13.5 to 22.0 h, respectively.

DISCUSSION

Studies have shown that the Isolator and BacT/Alert aerobic blood culture systems have performed as well as and, in most cases, better than other manual and automated broth-based systems. Henry and colleagues analyzed 11,567 blood culture

TABLE 2. Mean and median times for detection of growth and isolation of colonies

Group of organisms	Mean/median time (h)					
	Growth			Isolated colonies		
	$I(O_2)$	$BTA(O_2)$	Difference[a]	$BTA(O_2)$	$I(O_2)$	Difference[a]
Staphylococci	25.3/23.3	21.7/15.5	3.6/8.0	42.0/39.0	28.4/25.3	13.5/17.0
Streptococci	22.4/19.3	14.8/12.5	7.7/6.8	36.9/36.8	22.6/19.8	14.3/21.0
Enterobacteriaceae	18.1/16.5	17.0/12.5	1.1/3.0	37.1/37.8	18.1/16.5	19.0/23.0
Nonenteric gram-negative bacilli	27.8/24.5	21.2/19.5	6.5/7.5	41.8/41.5	27.8/24.5	14.0/23.0
Aerobic bacteria	23.1/19.5	19.5/14.5	3.6/4.0	40.3/39.0	24.0/19.5	21.5/16.3
Yeasts	35.6/35.0	31.2/27.0	4.4/3.0	54.3/51.0	35.6/35.0	22.0/18.7

[a] Between paired results [$BTA(O_2)$ and $I(O_2)$] ($P < 0.05$).

sets and demonstrated that the Isolator aerobic culture system recovered significantly more organisms ($P < 0.05$) than the aerobic (vented) Septi-Chek (Roche Diagnostics, Hoffmann-LaRoche, Inc., Nutley, N.J.) system. $I(O_2)$ recovered significantly more *Staphylococcus aureus* organisms ($P < 0.001$), while Septi-Chek recovered significantly more *Streptococcus pneumoniae* organisms ($P < 0.05$). $I(O_2)$ recovered the following organisms sooner: *S. aureus* ($P < 0.001$), *Pseudomonas aeruginosa* ($P < 0.001$), and *Candida* spp. ($P < 0.01$) (1).

Kirkley and colleagues recently compared a modification of Septi-Chek, Septi-Chek Release, an aerobic lysis-broth culture system (Becton Dickinson and Co., Hunt Valley, Md.), with $I(O_2)$ for 6,345 blood culture sets. The following organisms were detected more frequently by $I(O_2)$: *S. aureus* ($P = 0.0001$), *Alcaligenes xylosoxidans* ($P = 0.008$), *Klebsiella pneumoniae* ($P = 0.05$), *Salmonella* spp. ($P = 0.03$), and *Candida albicans* ($P = 0.02$). $I(O_2)$ also detected the following microorganisms sooner: *S. aureus* ($P = 0.0001$), *Enterococcus* spp. ($P = 0.0001$), *Enterobacter cloacae* ($P = 0.03$), *Escherichia coli* ($P = 0.0001$), *Klebsiella oxytoca* ($P = 0.03$), *K. pneumoniae* ($P = 0.02$), *P. aeruginosa* ($P = 0.002$), and *C. albicans* ($P = 0.005$) (4).

Quon and colleagues compared $BTA(O_2)$ with the aerobic Septi-Chek bottle. From 4,548 blood culture sets, the total recoveries by these two systems were equivalent. In addition, neither system identified any group or subgroup of organisms better than the other. However, $BTA(O_2)$ detected growth more rapidly overall (21 versus 37 h), most significantly for *S. aureus* (11.6 versus 30 h), viridans group streptococci (11.7 versus 22.4 h), *P. aeruginosa* (21.5 versus 33.5 h), and yeasts (34.4 versus 61.1 h) (5).

$BTA(O_2)$ was recently compared with the BACTEC 660 aerobic bottle by Wilson and colleagues, who analyzed 5,918 blood culture sets. The overall recoveries of microorganisms by these two aerobic bottles were comparable; however, organisms from the family *Enterobacteriaceae* were recovered more frequently by $BTA(O_2)$ alone ($P < 0.001$). Furthermore, growth of *S. aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.01$), streptococci ($P < 0.001$), *E. coli* ($P < 0.01$), other members of the family *Enterobacteriaceae* ($P < 0.02$), and *P. aeruginosa* ($P < 0.05$) was detected earlier by $BTA(O_2)$ (7).

In two recent reports, $I(O_2)$ was compared with the ESP automated blood culture system (Difco Laboratories, Detroit, Mich.) (2, 4). In a study of 10,535 blood cultures by Kirkley and colleagues with $I(O_2)$ and the ESP 80A aerobic bottle, significantly more positive cultures of *S. aureus* ($P < 0.001$), *Enterococcus* spp. ($P = 0.007$), *E. coli* ($P = 0.001$), *A. xylosoxidans* ($P = 0.02$), *Stenotrophomonas maltophilia* ($P = 0.01$), *C. albicans* ($P < 0.001$), and *Candida glabrata* ($P = 0.05$) were detected by $I(O_2)$ culture. Furthermore, $I(O_2)$ recovered *S. aureus* ($P < 0.001$) and *C. albicans* ($P < 0.001$) sooner (4). In a study of 7,070 blood cultures, Kellogg and colleagues found that more isolates of members of the family *Enterobacteriaceae* ($P < 0.001$), *E. coli* ($P < 0.01$), *K. pneumoniae* ($P < 0.01$), *P. aeruginosa* ($P < 0.05$), *S. aureus* ($P < 0.05$), and coagulase-negative staphylococci ($P < 0.001$) were detected by $I(O_2)$ culture than by ESP 80A aerobic culture (2).

Finally, Zwadyk and colleagues compared $BTA(O_2)$ with the ESP 80A aerobic bottle. For 5,421 compliant aerobic blood culture sets, ESP 80A detected significantly more *S. aureus* organisms ($P < 0.005$); otherwise, detection frequencies for other microorganisms were similar (8).

In this study, the total recovery of microorganisms by $BTA(O_2)$ was nearly the same as the total recovery by $I(O_2)$. $I(O_2)$ alone recovered more isolates of *S. aureus* and coagulase-negative staphylococci than did $BTA(O_2)$, but these differences achieved statistical significance only when all staphylococci were analyzed as a group ($P < 0.05$). Similarly, by itself $BTA(O_2)$ recovered as many or more isolates of every aerobic and facultatively anaerobic gram-negative bacillus species identified (except *Proteus rettgeri*), but these differences achieved statistical significance only when aerobic and facultatively anaerobic gram-negative bacilli were analyzed as a group ($P < 0.05$). $I(O_2)$ recovered a significantly greater number of yeast isolates ($P < 0.01$), but this difference was largely a consequence of reduced recovery of *Candida parapsilosis* by $BTA(O_2)$ (Table 1). $BTA(O_2)$ identified growth significantly more rapidly for all organisms (considered as a group) than did $I(O_2)$. This difference likely reflected the nearly continuous monitoring (every 10 min) of bottles in the BacT/Alert incubator. $I(O_2)$ plates were manually checked less frequently, as described above. In contrast, the time for isolation of colonies occurred sooner with the $I(O_2)$ system.

C. parapsilosis isolates were recovered from five patients. Impaired recovery of *C. parapsilosis* from blood by BacT/Alert has not previously been reported. Further study of the growth of *C. parapsilosis* in the BacT/Alert system is planned.

In summary of this study, overall recoveries by $BTA(O_2)$ and $I(O_2)$ were similar. As was the case in many previous studies, $I(O_2)$ recovered more staphylococcus and yeast isolates. However, $BTA(O_2)$ recovered more aerobic and facultatively anaerobic gram-negative bacilli, compared with $I(O_2)$. For organisms recovered by both systems, $BTA(O_2)$ identified growth more rapidly while $I(O_2)$ produced isolated colonies for identification and susceptibility testing significantly more rapidly. These data suggest that a combination of the $BTA(O_2)$ and $I(O_2)$ blood culture systems would optimize the recovery of microorganisms from blood. A combination of $BTA(O_2)$ and

$I(O_2)$, in addition to the BTA anaerobic bottle, may be particularly appealing for laboratories that use high volumes of blood (i.e., 30 ml) per blood culture set and a three-component blood culture system. For laboratories that use smaller amounts of blood and have very low frequencies of anaerobic bacteremia, a combination of the $BTA(O_2)$ and $I(O_2)$ blood culture systems may be useful. However, the cost effectiveness of using these two blood culture systems together requires further evaluation. The laboratory costs for instruments, reagents, and processing of blood cultures must be weighted with potential cost savings for patients whose bloodstream infections may be more reliably and rapidly diagnosed by using a combination of the $BTA(O_2)$ and $I(O_2)$ systems.

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