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Controlled Comparison of the BacT/Alert and BACTEC 660/730 Nonradiometric Blood Culture Systems

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In a collaborative study at three university hospitals, the recovery of microorganisms and the speed of detection of microbial growth by the BacT/Alert (Organon Teknika Corporation, Durham, N.C.) and BACTEC 660/730 (Becton-Dickinson Diagnostic Instrument Systems, Sparks, Md.) nonradiometric blood culture systems were compared. A total of 5,918 comparisons were made between BacT/Alert aerobic and BACTEC NR 6A bottles and 5,992 comparisons were made between BacT/Alert anaerobic and BACTEC NR 7A bottles. Each bottle was inoculated with 5 ml of blood. The overall recoveries of microorganisms from the two aerobic bottles were comparable; members of the family *Enterobacteriaceae* were recovered more often from BacT/Alert aerobic bottles alone ($P < 0.001$). The overall recoveries of microorganisms from the two anaerobic bottles were not significantly different. Growth of *Staphylococcus aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.01$), streptococci ($P < 0.001$), *Escherichia coli* ($P < 0.01$), other members of the family *Enterobacteriaceae* ($P < 0.02$), and *Pseudomonas aeruginosa* ($P < 0.05$) was detected earlier in BacT/Alert aerobic bottles. Growth of *S. aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.05$), enterococci ($P < 0.01$), *Streptococcus pneumoniae* ($P < 0.02$), viridans group streptococci ($P < 0.05$), *E. coli* ($P < 0.001$), *Klebsiella pneumoniae* ($P < 0.01$), and other members of the family *Enterobacteriaceae* ($P < 0.001$) was detected earlier in BacT/Alert anaerobic bottles. In a system-versus-system comparison, more gram-positive cocci were recovered from the BACTEC system alone ($P < 0.05$), and more members of the family *Enterobacteriaceae* were recovered from the BacT/Alert system alone ($P < 0.001$). As a system, the BacT/Alert system detected growth of *S. aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.01$), streptococci ($P < 0.001$), *E. coli* ($P < 0.001$), other members of the family *Enterobacteriaceae* ($P < 0.001$), and *P. aeruginosa* ($P < 0.05$) earlier than the BACTEC system did. Significantly fewer (40 versus 1,183) false-positive results occurred with the BacT/Alert system. We conclude that the BacT/Alert and BACTEC 660/730 nonradiometric systems are comparable for recovering clinically significant microorganisms from adult patients with bacteremia or fungemia, but that the BacT/Alert system detects microbial growth earlier than the BACTEC system does, with significantly fewer false-positive results.

Several commercial automated systems for detecting microbial growth in blood culture bottles have been developed during the past 20 years. These systems vary in the methodologies they use for detecting microbial growth, the types of broth media and media supplements available for use with each system, bottle atmospheres, the blood-to-broth ratio in inoculated bottles, the volume of blood that can be inoculated into each bottle, and the use of shakers or other agitation for processing aerobic bottles. To date, the most widely used of these systems have been the BACTEC 460 radiometric and 660/730 nonradiometric systems (Becton-Dickinson Diagnostic Instrument Systems, Sparks, Md.). BACTEC systems have been in use for many years, and their diagnostic strengths and limitations are well characterized.

More recently, Organon Teknika Corporation (Durham, N.C.) introduced BacT/Alert, an automated microbial detection system designed to detect microbial growth in blood culture bottles (16). Although the BacT/Alert system also detects microbial growth by monitoring changes in CO_2 concentration as microorganisms grow in blood culture bottles, it differs from the BACTEC systems in several ways. The primary differences are that the BacT/Alert system uses a colorimetric detection methodology, tests each bottle once every 10 min, agitates both aerobic and anaerobic bottles throughout the incubation period, and uses a growth detection algorithm that monitors each bottle for an increasing rate of change and/or sustained increase in CO_2 concentration (16). The incubation, agitation, and detection mechanisms are contained in a single unit (16).

Results of a limited clinical trial with a prototype research instrument showed that the BacT/Alert system was comparable to the BACTEC 460 radiometric blood culture system in its ability to detect microorganisms in blood culture bottles and that large-scale clinical trials with commercial versions of the system were warranted (16). We report the results of such a collaborative trial conducted at three university hospitals in which the BacT/Alert system was compared with the BACTEC 660/730 nonradiometric blood culture system by using bottles inoculated with 5 ml of blood from adult patients with suspected bacteremia or fungemia.

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MATERIALS AND METHODS

Comparisons and analyses. During the study period, the BacT/Alert and BACTEC 660/730 nonradiometric blood culture systems were used to process blood cultures drawn from adult patients with suspected bacteremia or fungemia at Duke University Medical Center, the Robert Wood Johnson University Hospital, and the Salt Lake City Department of Veterans Affairs Medical Center. For each blood culture, one aerobic and one anaerobic bottle from each system was inoculated with 5 ml of blood. The following three separate comparisons were performed with data collected during the study: BacT/Alert aerobic bottles versus BACTEC NR 6A bottles, BacT/Alert anaerobic versus BACTEC NR 7A bottles, and a system-versus-system comparison (i.e., a comparison of the combination of BacT/Alert aerobic and anaerobic bottles versus the combination of BACTEC NR 6A and BACTEC NR 7A bottles when all four bottles were inoculated with blood from a single venipuncture). Each comparison consisted of analyses for the recovery of microorganisms (yield) and the relative speed of detection of microbial growth.

Blood culture systems. BacT/Alert blood culture bottles contain 40 ml of supplemented tryptic soy broth with 0.035% sodium polyanetholesulfonate (SPS) as an anticoagulant. The atmosphere in BacT/Alert aerobic bottles contains CO_2 in air, and the atmosphere in BacT/Alert anaerobic bottles contains CO_2 in nitrogen. BacT/Alert bottles rock continuously at a rate of 68 cycles per min and are incubated at 35 to 37°C for 7 days or until they are positive. BACTEC NR 6A and NR 7A bottles contain 30 ml of tryptic soy broth with 0.03% SPS. The atmosphere in BACTEC NR 6A bottles contains CO_2 in oxygen, and the atmosphere in BACTEC NR 7A bottles contains CO_2 in nitrogen. BACTEC NR 6A bottles are agitated on an orbital shaker for the first 24 to 48 h at a rate of 280 rpm, after which they incubate for another 5 days without agitation. BACTEC NR 7A anaerobic bottles are not agitated. All BACTEC bottles are incubated at 35 to 37°C throughout processing.

Blood culture collection. The skin of the patients was disinfected by standard techniques (13). Twenty milliliters of blood was collected at the bedside, and 5 ml was immediately inoculated into each of the four blood culture bottles in the following order: BACTEC NR 6A bottle, BACTEC NR 7A bottle, BacT/Alert aerobic bottle, and BacT/Alert anaerobic bottle. The BACTEC NR 6A and NR 7A bottles were inoculated first to ensure that, for each patient, a blood culture was performed with the reference system even in those instances in which less than 20 ml of blood was obtained.

Laboratory processing. All study bottles were compared against standards with known volumes, and the adequacy of fill for each bottle was recorded as follows: <4 ml, inadequate; 4 to 6 ml, adequate; >6 ml, overfilled. Only adequately filled bottles were analyzed for study purposes, although all bottles containing blood were processed for purposes of patient care. Bottles with macroscopic evidence of growth were not placed in the respective instrument but were Gram stained and subcultured. The time of receipt of all bottles was considered to be the time when the BacT/Alert bottles were entered into the BacT/Alert system, irrespective of the time of collection. Bottles placed in the instruments were processed and tested according to the recommendations of each manufacturer. BACTEC NR 6A bottles were tested twice daily on the first 2 days of incubation and once daily thereafter through day 7. BACTEC NR 7A bottles were tested once daily through day 7. Although BacT/Alert instruments continuously monitor bottles for microbial growth, the three study sites standardized processing by checking the instruments for positive results at five different times (0800, 1000, 1200, 1400, and 2000 h) on weekdays and three different times (0800, 1200, and 1400 h) on weekends. Organisms were cultured and identified by standard microbiological procedures (3). When a microorganism was recovered by only one system, subcultures were performed at the end of incubation on negative bottles in the other system. The means by which growth was detected (macroscopic evidence, absolute growth values, changes in growth values, rate of change of CO_2 production, or terminal subculture) and the time required to detect growth were recorded for each positive bottle. The time required to detect growth in BacT/Alert bottles was calculated by subtracting the time of receipt (as defined above) from the time of detection recorded by the BacT/Alert instrument. The time required to detect growth in BACTEC bottles was calculated by subtracting the time of receipt from the time at which positive bottles were tested.

Clinical assessment. Positive cultures were reviewed by a physician who specialized in infectious diseases. The microorganisms isolated were judged, on the basis of published criteria (18), to be contaminants, etiologic agents of bacteremia or fungemia, or indeterminate as the cause of sepsis.

Data analysis. Only results from bottles adequately filled with blood and in which microorganisms judged to represent true bacteremia or fungemia grew were analyzed. Comparisons were evaluated statistically by a modified chi-square test with Yates' correction for small numbers of observations when appropriate (11). Data were collated and analyzed at the Clinical Microbiology Laboratory at Duke University Medical Center.

RESULTS

A total of 7,924 blood culture bottle sets were received during the study period. Of these, 5,918 were received with both aerobic bottles adequately filled and 5,992 were received with both anaerobic bottles adequately filled. Together, the two aerobic bottles yielded 364 clinically significant isolates and the two anaerobic bottles yielded 337 clinically significant isolates. Of the microorganisms isolated from the two aerobic bottles, 230 of 364 (63.2%) were recovered from both bottles, 59 (16.2%) from BACTEC NR 6A bottles only and 76 (20.9%) from BacT/Alert aerobic bottles only (Table 1). Members of the family *Enterobacteriaceae* were recovered more often from BacT/Alert aerobic bottles alone ($P < 0.001$), but the overall recoveries from the two aerobic bottles were not significantly different. Of the microorganisms isolated from the two anaerobic bottles, 204 of 337 (60.5%) were recovered from both bottles, 57 (16.9%) from BACTEC NR 7A bottles only and 76 (22.6%) from BacT/Alert anaerobic bottles only (Table 2). The overall recoveries of microorganisms from the two anaerobic bottles were not significantly different, nor were there significant differences in the ability of the two bottles to recover specific microorganisms.

Of the 230 isolates recovered from both aerobic bottles, 11 (4.8%) were recovered simultaneously from both bottles, 46 (20.0%) were recovered earlier from BACTEC NR 6A bottles, and 173 (75.2%) were recovered earlier from BacT/Alert aerobic bottles ($P < 0.001$) (Table 3). *Staphylococcus aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.01$), streptococci ($P < 0.001$), *Escherichia coli* ($P < 0.01$),

TABLE 1. Comparative yields of clinically important bacteria and fungi in BacT/Alert and BACTEC NR 6A aerobic blood culture bottles

Microorganism	No. of isolates recovered from:			P
	Both bottles	BACTEC NR 6A only	BacT/Alert only	
S. aureus	73	8	8	NS[a]
Coagulase-negative staphylococci	34	14	8	NS
Enterococci	13	5	2	NS
Streptococci[b]	15	9	6	NS
Other gram-positive bacteria[c]	1	0	1	NS
Enterobacteriaceae[d]	56	10	29	<0.01
P. aeruginosa	6	4	3	NS
Other gram-negative bacteria[e]	4	1	2	NS
Anaerobic bacteria[f]	3	0	4	NS
C. albicans	11	2	4	NS
Other fungi[g]	14	5	9	NS
All microorganisms	230	59	76	NS

[a] NS, not significant ($P > 0.05$).
[b] Includes 2 group B and 4 group G streptococci, 10 *Streptococcus pneumoniae*, 10 viridans group streptococci, and 4 unidentified (not group A) beta-hemolytic streptococci.
[c] Includes two *Corynebacterium* group JK.
[d] Includes 2 *Citrobacter* spp., 3 *Enterobacter aerogenes*, 8 *Enterobacter cloacae*, 41 *Escherichia coli*, 8 *Klebsiella oxytoca*, 17 *Klebsiella pneumoniae*, 2 *Morganella morganii*, 4 *Proteus mirabilis*, 1 *Proteus* spp., 5 *Serratia marcescens*, 2 *Serratia liquefaciens*, and 2 *Salmonella typhi*.
[e] Includes two *Acinetobacter* spp., one *Acaligenes* sp., two *Neisseria meningitidis*, and two *Xanthomonas maltophilia*.
[f] Includes one *Clostridium tertium*, two *Clostridium perfringens*, two *Clostridium* spp., one unidentified anaerobic gram-positive bacillus, and one culture with mixed anaerobic bacteria.
[g] Includes 3 *Cryptococcus neoformans*, 5 *Candida parapsilosis*, 10 *Candida tropicalis*, 1 *Candida* sp., and 9 *Torulopsis glabrata*.

TABLE 2. Comparative yields of clinically important bacteria and fungi in BacT/Alert and BACTEC NR 7A anaerobic blood culture bottles

Microorganism	No. of isolates recovered from:			P
	Both bottles	BACTEC NR 7A only	BacT/Alert only	
S. aureus	70	7	14	NS[a]
Coagulase-negative staphylococci	22	13	11	NS
Enterococci	10	6	5	NS
Streptococci[b]	19	9	4	NS
Other gram-positive bacteria[c]	0	0	1	NS
Enterobacteriaceae[d]	56	11	21	NS
P. aeruginosa	1	1	3	NS
Other gram-negative bacteria[e]	0	1	1	NS
Anaerobic bacteria[f]	19	6	8	NS
C. albicans	2	1	3	NS
Other fungi[g]	5	2	5	NS
All microorganisms	204	57	76	NS

[a] NS, not significant ($P > 0.05$).
[b] Includes 2 group A, 1 group B, and 3 group G streptococci; 11 *Streptococcus pneumoniae*; 8 viridans group streptococci; and 7 unidentified (not group A) beta-hemolytic streptococci.
[c] Includes one *Listeria* sp.
[d] Includes 2 *Citrobacter freundii*, 3 *Citrobacter diversus*, 1 *Enterobacter aerogenes*, 10 *Enterobacter cloacae*, 41 *Escherichia coli*, 2 *Klebsiella oxytoca*, 13 *Klebsiella pneumoniae*, 2 *Morganella morganii*, 3 *Proteus mirabilis*, 1 *Proteus* sp., 5 *Serratia marcescens*, 2 *Serratia liquefaciens*, 2 *Salmonella typhi*, and 1 *Salmonella* spp.
[e] Includes one *Acinetobacter* sp. and one *Xanthomonas maltophilia*.
[f] Includes one *Clostridium tertium*, two *Clostridium ramosum*, four *Clostridium perfringens*, five *Clostridium* spp., four unidentified anaerobic gram-positive bacilli, one *Eubacterium limosum*, five *Bacteroides fragilis*, one *Bacteroides fragilis* group, one *Bacteroides melaninogenicus*, one *Bacteroides ovatus*, two *Bacteroides thetaiotaomicron*, two *Bacteroides* spp., two *Fusobacterium* spp., and two cultures with mixed anaerobic bacteria.
[g] Includes three *Candida tropicalis* and nine *Torulopsis glabrata*.

other members of the family *Enterobacteriaceae* ($P < 0.02$), and *Pseudomonas aeruginosa* ($P < 0.05$) were each recovered first from BacT/Alert aerobic bottles. The overall difference in the speed of detection with the two aerobic bottles is illustrated in Fig. 1 as the cumulative percent positive cultures plotted against time throughout the 7-day incubation period.

Of the 204 isolates recovered from both anaerobic bottles, 3 (1.5%) were recovered simultaneously from both bottles, 25 (12.3%) were recovered first from BACTEC NR 7A bottles, and 176 (86.3%) were recovered first from BacT/Alert anaerobic bottles ($P < 0.001$) (Table 4). *S. aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.05$), enterococci ($P < 0.01$), viridans group streptococci ($P < 0.05$), *Streptococcus pneumoniae* ($P < 0.02$), *E. coli* ($P < 0.001$), *Klebsiella pneumoniae* ($P < 0.01$), and other members of the family *Enterobacteriaceae* ($P < 0.001$) were each recovered first from BacT/Alert anaerobic bottles. The overall difference in the speed of detection with the two anaerobic bottles is illustrated in Fig. 2, which is the cumulative percent positive cultures plotted against time throughout the 7-day incubation period.

A total of 135 terminal subcultures were performed when isolates were recovered in one system but not the other by the end of the 7-day incubation period. Eight of these were positive, two with BacT/Alert bottles and six with BACTEC bottles. Four of six isolates detected by terminal subculture with BACTEC bottles were recovered from NR 6A bottles and two of six were recovered from NR 7A BACTEC bottles. For BacT/Alert bottles, one isolate was recovered from an aerobic bottle and the other from an anaerobic bottle. Three isolates recovered by terminal subculture were bacteria (one each of *Bacteroides fragilis* group, *Fusobacterium* sp., and *Corynebacterium* group JK), and five were yeasts (two *Candida albicans*, one *Candida parapsilosis*, and two *Torulopsis glabrata*).

In the system-versus-system comparison, 5,389 sets were received in which all four bottles were adequately filled. The overall recoveries of microorganisms were not significantly different between the two systems ($P > 0.05$) (Table 5). For specific microorganisms, the BacT/Alert system recovered significantly more members of the family *Enterobacteriaceae* ($P < 0.01$). In contrast, the BACTEC system recovered significantly more facultative and aerobic gram-positive cocci ($P < 0.05$).

In the system-versus-system comparison, growth of *S. aureus* ($P < 0.001$), coagulase-negative staphylococci ($P < 0.01$), streptococci ($P < 0.001$), *E. coli* ($P < 0.001$), other members of the family *Enterobacteriaceae* ($P < 0.001$), *P. aeruginosa* ($P < 0.05$), and all microorganisms combined ($P < 0.001$) was detected first on BacT/Alert instruments (Table 6).

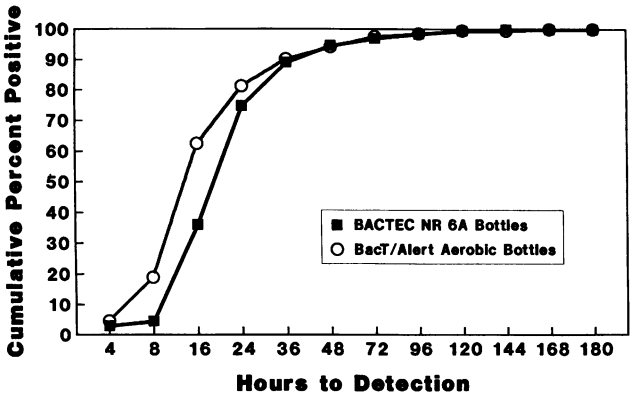

FIG. 1. Cumulative recoveries of all microorganisms from BACTEC NR 6A and BacT/Alert aerobic blood culture bottles during the 7-day incubation period.

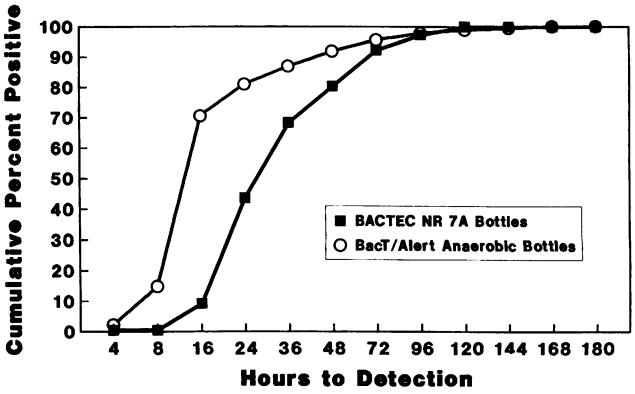

FIG. 2. Cumulative recoveries of all microorganisms from BACTEC NR 7A and BacT/Alert anaerobic blood culture bottles during the 7-day incubation period.

During the study period, 1,183 false-positive results (i.e., an instrument gave a positive signal on a bottle but Gram stains and subcultures of that bottle were negative) occurred during testing of study bottles on BACTEC instruments at the study sites. Of these, 700 occurred with aerobic bottles and 483 occurred with anaerobic bottles. In comparison, 40 false-positive results occurred during testing of study bottles on BacT/Alert instruments at the study sites. Of these, 22 occurred with aerobic bottles and 18 occurred with anaerobic bottles.

DISCUSSION

This multicenter controlled evaluation compared aerobic and anaerobic BacT/Alert blood culture bottles against the reference BACTEC NR 6A and NR 7A bottles inoculated with equal volumes of blood from adult patients with suspected bacteremia or fungemia. Simultaneous inoculation of all four bottles from single blood cultures also enabled a system-versus-system comparison of the BacT/Alert and BACTEC nonradiometric 660/730 instruments.

With the exception of members of the family *Enterobacteriaceae*, which were recovered significantly more often from BacT/Alert aerobic bottles alone, there were no significant differences in yield between BacT/Alert and BACTEC bottles in either the aerobic or the anaerobic bottle-versus-bottle comparison.

Although BacT/Alert and BACTEC bottles were found to be comparable for recovering microorganisms, BacT/Alert detected microbial growth in both aerobic and anaerobic bottles significantly earlier than the BACTEC instruments did. Earlier detection of microbial growth by BacT/Alert probably was due to the detection algorithm (16). Unlike BACTEC instruments, which depend upon numeric threshold and delta values to categorize bottle readings as positive or negative, BacT/Alert instruments analyze the growth curves generated for each bottle either for an increasing rate of change or a sustained increase in CO_2 concentration. Such changes in CO_2 concentration occur before arbitrary numeric threshold values in CO_2 concentration can be exceeded, and thus microbial growth is detected earlier.

Only eight isolates were recovered when terminal subcultures were performed. These results are consistent with previous reports that neither blind subcultures (9, 10) nor terminal subcultures are necessary with BACTEC blood culture bottles (1). These data also indicate that terminal subcultures are not necessary with the BacT/Alert system. In this study terminal subcultures were performed only when growth was detected in one system but not the other by the end of the 7-day incubation period. Therefore, we did not attempt to identify isolates which would have been detected only by terminal subculture (i.e., when all bottles were negative in both systems). Isolation by terminal subculture was so infrequent (8 of 135, or 59%), even when microorganisms were known to be present in the blood, however, that it is unlikely that a significant number of isolates would remain undetected by either system if terminal subcultures were not performed. Of additional interest is the fact that five of eight microorganisms detected by terminal subcultures were yeasts. As reported previously (13), in certain instances optimal recovery of yeasts and fastidious bacteria such as members of the genera *Neisseria*, *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, and *Eikenella* may require terminal subculture and/or prolonged incubation.

Overall differences in yield were not found when BacT/Alert and BACTEC were compared as systems. However, significantly more members of the family *Enterobacteriaceae* were recovered by the BacT/Alert system, and significantly more aerobic and facultatively anaerobic gram-positive cocci were recovered by the BACTEC system. The reason(s) for these selective discrepancies in recovery is not known. Although BacT/Alert bottles contain slightly more SPS (0.035 versus 0.030%) compared with that in BACTEC system media, and higher concentrations of SPS are known to increase recoveries of gram-negative bacteria (4) while at the same time they may decrease the recovery of gram-positive cocci (6, 17), the differences in SPS concentrations probably were not sufficient to explain the differences in recoveries. The broth medium used with each system is based on a soybean-casein digest medium containing nutritional supplements. Although the specific recipe for each broth medium is proprietary, it is unlikely that differences in media formulation alone accounted for our observations, particularly since the differences in recoveries were limited to only two groups of bacteria.

Significantly fewer false-positive results occurred with BacT/Alert instruments than with BACTEC instruments. The BACTEC and BacT/Alert instruments used at the study sites during the study period were used according to the recommendations and specifications of each manufacturer. Significant malfunctions did not occur with any of the instruments, nor were any instruments modified during the

TABLE 3. Comparative speeds of detection of clinically important bacteria and fungi in BacT/Alert and BACTEC NR 6A aerobic blood culture bottles

Microorganism	Growth detected in (no. of isolates): BacT/Alert and BACTEC NR 6A at same time	BACTEC NR 6A earlier	BacT/Alert earlier	P
S. aureus	2	10	61	<0.001
Coagulase-negative staphylococci	1	9	24	<0.01
Enterococci	0	4	9	NS[a]
Streptococci[b]	0	1	14	<0.001
Other gram-positive bacteria[c]	0	0	1	NS
E. coli	4	3	16	<0.01
K. pneumoniae	0	2	9	NS
Other *Enterobacteriaceae*[d]	4	5	17	<0.02
P. aeruginosa	0	0	6	<0.05
Other gram-negative bacteria[e]	0	0	4	NS
Anaerobic bacteria[f]	0	0	3	NS
C. albicans	1	7	3	NS
Other fungi[g]	3	5	6	NS
All microorganisms	11	46	173	<0.001

[a] NS, not significant ($P > 0.05$).
[b] Includes two group G streptococci, seven *Streptococcus pneumoniae*, five viridans group streptococci, and one unidentified (not group A) beta-hemolytic streptococcus.
[c] Includes one *Corynebacterium* group JK.
[d] Includes one *Citrobacter freundii*, one *Citrobacter diversus*, one *Enterobacter aerogenes*, six *Enterobacter cloacae*, one *Klebsiella oxytoca*, two *Morganella morganii*, one *Proteus mirabilis*, four *Serratia marcescens*, two *Serratia liquefaciens*, and two *Salmonella typhi*.
[e] Includes one *Acinetobacter* sp., one *Xanthomonas maltophilia*, and two *Neisseria meningitidis*.
[f] Includes one *Clostridium* sp., one *Clostrium perfringens*, and one unidentified anaerobic gram-positive bacillus.
[g] Includes three *Candida parapsilosis*, four *Candida tropicalis*, three *Cryptococcus neoformans*, and four *Torulopsis glabrata*.

TABLE 4. Comparative speeds of detection of clinically important bacteria and fungi in BacT/Alert and BACTEC NR 7A anaerobic blood culture bottles

Microorganism	Growth detected in (no. of isolates): BacT/Alert and BACTEC NR 7A at same time	BACTEC NR 7A earlier	BacT/Alert earlier	P
S. aureus	1	7	62	<0.001
Coagulase-negative staphylococci	0	6	16	<0.05
Enterococci	0	0	10	<0.01
S. pneumoniae	0	0	8	<0.02
Viridans group streptococci	0	0	6	<0.05
Other streptococci[a]	0	0	5	NS[b]
E. coli	1	1	25	<0.001
K. pneumoniae	0	0	9	<0.01
Other *Enterobacteriaceae*[c]	0	1	19	<0.001
P. aeruginosa	0	1	0	NS
Anaerobic bacteria[d]	0	9	10	NS
C. albicans	1	0	1	NS
Other fungi[e]	0	0	5	NS
All microorganisms	3	25	176	<0.001

[a] Includes one group A and two group G streptococci and two unidentified (not group A) beta-hemolytic streptococci.
[b] NS, not significant ($P > 0.05$).
[c] Includes one *Citrobacter freundii*, two *Citrobacter diversus*, one *Enterobacter aerogenes*, six *Enterobacter cloacae*, two *Morganella morganii*, one *Proteus mirabilis*, one *Proteus* sp., three *Serratia marcescens*, two *Salmonella typhi*, and one *Salmonella* sp.
[d] Includes two *Clostridium perfringens*, two *Clostridium ramosum*, four *Clostridium* spp., two *Bacteroides fragilis*, one *Bacteroides fragilis* group, one *Bacteroides melaninogenicus*, one *Bacteroides ovatus*, two *Bacteroides thetaiotaomicron*, one *Bacteroides* sp., and three unidentified anaerobic gram-positive bacilli.
[e] Includes one *Candida tropicalis* and four *Torulopsis glabrata*.

study. BACTEC threshold and delta values used at each study site were based specifically on recommendations by the manufacturer to maximize true-positive signals and to minimize false-positive signals. No adjustments to these values were made, in order to maintain uniform experimental conditions throughout the study at each study site. Although under routine clinical laboratory conditions BACTEC threshold and delta values could be modified to reduce the number of false-positive signals, it is unlikely that they could be modified sufficiently to decrease false-positive signals to the number generated by the BacT/Alert system. Moreover, such modifications would simultaneously decrease the sensitivity of the BACTEC system, potentially resulting in delayed or missed detection of microbial growth. The lower number of false-positive results associated with the BacT/Alert system is probably due to the computer algorithm used by the instrument to detect microbial growth. BacT/Alert bottles must attain either an increased rate of change or a sustained (linear) increase in the CO_2 concentration to be classified as positive, and background increases in the CO_2 concentration (such as production of CO_2 by leukocytes) usually do not meet these criteria (16). In contrast, background increases in the CO_2 concentration can exceed the numeric threshold values used on BACTEC instruments, resulting in false-positive signals.

The BacT/Alert detection mechanism does not require sampling of bottle contents, and therefore, bottle atmospheres are not replenished during incubation and testing. Recovery of strictly aerobic or anaerobic microorganisms from BacT/Alert bottles might therefore be expected to be inferior relative to recovery from BACTEC bottles, in which atmospheres are replenished at each sampling time and thus presumably have more well-preserved aerobic and anaerobic conditions within each bottle. Such differences in the recoveries of strictly aerobic or anaerobic microorganisms were not observed in this study, since strictly aerobic microorganisms such as *P. aeruginosa* (8) and *C. albicans* were recovered with equal frequencies from both BacT/Alert and BACTEC bottles. Furthermore, although the number of isolates was small, there were no significant differences in the recovery of anaerobic bacteria between the two systems.

In summary, this multicenter controlled comparison found the yields for BacT/Alert aerobic and anaerobic blood culture bottles to be comparable to those for BACTEC NR 6A and NR 7A bottles. However, the BacT/Alert system detected microbial growth before the BACTEC system did for a wide variety of pathogenic bacteria isolated in both aerobic

TABLE 5. Comparative yields of clinically important bacteria and fungi in BacT/Alert and BACTEC blood culture systems

Microorganism	No. of isolates recovered from:			P
	Both systems	BACTEC only	BacT/Alert only	
S. aureus	76	8	8	NS[a]
Coagulase-negative staphylococci	40	16	8	NS
Enterococci	15	6	2	NS
Streptococci[b]	23	9	3	NS
Other gram-positive bacteria[c]	0	0	2	NS
All gram-positive bacteria	154	39	23	<0.05
Enterobacteriaceae[d]	69	7	23	<0.01
P. aeruginosa	7	4	2	NS
Other gram-negative bacteria[e]	4	0	2	NS
Anaerobic bacteria[f]	16	5	9	NS
Yeasts[g]	24	8	13	NS
All microorganisms	274	63	72	NS

[a] NS, not significant ($P > 0.05$).

[b] Includes 1 group A, 3 group B, and 3 group G streptococci; 23 *Enterococcus* spp., 12 *Streptococcus pneumoniae*; 10 viridans group streptococci; and 6 unidentified (not group A) beta-hemolytic streptococci.

[c] Includes one *Corynebacterium* group JK and one *Listeria monocytogenes*.

[d] Includes 4 *Citrobacter* spp., 2 *Enterobacter aerogenes*, 10 *Enterobacter cloacae*, 43 *Escherichia coli*, 8 *Klebsiella oxytoca*, 16 *Klebsiella pneumoniae*, 2 *Morganella morganii*, 4 *Proteus mirabilis*, 1 *Proteus* sp., 2 *Serratia liquefaciens*, 5 *Serratia marcescens*, and 2 *Salmonella* spp.

[e] Includes one *Alcaligenes* sp., one *Acinetobacter* sp., two *Xanthomonas maltophilia*, and two *Neisseria meningitidis*.

[f] Includes one *Clostridium tertium*, four *Clostridium perfringens*, five *Clostridium* spp., one *Eubacterium limosum*, three unidentified gram-positive bacilli, five *Bacteroides fragilis*, one *Bacteroides fragilis* group, one *Bacteriodes melaninogenicus*, one *Bacteroides ovatus*, two *Bacteriodes thetaiotaomicron*, two *Bacteroides* spp., two *Fusobacterium* spp., and two cultures with mixed anaerobic bacteria.

[g] Includes 16 *Candida albicans*, 3 *Cryptococcus neoformans*, 5 *Candida parapsilosis*, 10 *Candida tropicalis*, 1 *Candida* spp., and 10 *Torulopsis glabrata*.

TABLE 6. Comparative speeds of detection of clinically important bacteria and fungi in BacT/Alert and BACTEC blood culture systems

Microorganism	Growth detected in (no. of isolates):			P
	BACTEC and BacT/Alert at same time	BACTEC earlier	BacT/Alert earlier	
S. aureus	2	18	81	<0.001
Coagulase-negative staphylococci	1	15	34	<0.01
Enterococci	0	5	12	NS
Streptococci[a]	0	3	23	<0.001
Other gram-positive bacteria[b]	0	0	2	NS[c]
E. coli	8	6	34	<0.001
Other *Enterobacteriaceae*[d]	1	9	44	<0.001
P. aeruginosa	0	1	8	<0.05
Other gram-negative bacteria[e]	1	2	7	NS
Anaerobic bacteria[f]	2	10	11	NS
Candida albicans	1	10	5	NS
Other fungi[g]	3	7	10	NS
All microorganisms	19	86	271	<0.001

[a] Includes 1 group A and 3 group G streptococci, 11 *Streptococcus pneumoniae*, 8 viridans group streptococci, and 3 unidentified (not group A) beta-hemolytic streptococcus.

[b] Includes two *Corynebacterium* group JK.

[c] NS, not significant ($P > 0.05$).

[d] Includes 2 *Citrobacter freundii*, 2 *Citrobacter diversus*, 3 *Enterobacter aerogenes*, 9 *Enterobacter cloacae*, 3 *Klebsiella oxytoca*, 17 *Klebsiella pneumoniae*, 2 *Morganella morganii*, 4 *Proteus mirabilis*, 1 *Proteus* sp., 5 *Serratia marcescens*, 2 *Serratia liquefaciens*, 2 *Salmonella typhi*, and 2 *Salmonella* spp.

[e] Includes five *Acinetobacter* sp., two *Pseudomonas cepacia*, one *Xanthomonas maltophilia*, and two *Neisseria meningitidis*.

[f] Includes three *Clostridium perfringens*, two *Clostridium ramosum*, four *Clostridium* spp., three unidentified anaerobic gram-positive bacilli, two *Bacteroides fragilis*, one *Bacteroides fragilis* group, one *Bacteroides melaninogenicus*, one *Bacteroides ovatus*, two *Bacteroides thetaiotaomicron*, one *Bacteroides* sp., two *Fusobacterium* spp., and one culture with mixed anaerobic bacteria.

[g] Includes 16 *Candida albicans*, 4 *Candida parapsilosis*, 4 *Candida tropicalis*, 3 *Cryptococcus neoformans*, and 9 *Torulopsis glabrata*.

and anaerobic bottles. In the system-versus-system comparison, the BacT/Alert and BACTEC systems were found to have comparable yields, but the BacT/Alert system was found to detect microbial growth earlier. The BacT/Alert system produced significantly fewer false-positive results than the BACTEC system did. Terminal subcultures were shown to be unnecessary with either system.

It should be emphasized that this comparison of BacT/Alert with the BACTEC 660/730 nonradiometric blood culture system was limited to a comparison of the currently available BacT/Alert bottles against BACTEC NR 6A and 7A bottles and that this study was not designed to address other issues relevant to the BacT/Alert system. For example, although BacT/Alert bottles can accept blood inocula of up to 10 ml, BacT/Alert bottles containing more than 6 ml of blood were excluded from this study. Given the importance of volume in detecting bacteremia and fungemia in adults (2, 5, 7, 12, 14, 15), large-scale clinical trials comparing BacT/Alert bottles with other blood culture bottles designed to accept up to 10 ml of blood are needed. Other issues requiring additional investigation include evaluation of the BacT/Alert system for detecting bacteremia and fungemia in children, determining the ability of the BacT/Alert system to recover microorganisms from patients receiving antimicrobial therapy, and determining the ability of the BacT/Alert system to recover fastidious microorganisms not encountered during this study.

This study demonstrated that the BacT/Alert system detects microbial growth earlier than the BACTEC system does with significantly fewer false-positive results. These findings, coupled with design features currently unique to BacT/Alert, suggest that use of the BacT/Alert system might be expected to reduce laboratory work load. Studies to determine whether the use of the BacT/Alert system in clinical microbiology laboratories reduces work load and/or costs should be performed. The magnitude of the speed advantage of the BacT/Alert system will be most apparent in laboratories in which microbiology technologists are present during all shifts. Conversely, the speed advantage will not be as great in laboratories with single-shift microbiology services. Moreover, the impact of earlier detection of microbial growth on patient care and/or reductions in costs associated with such care has yet to be ascertained. Given current

concerns with cost containment, studies to evaluate these issues appear to be warranted.

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