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Comparative Evaluation of Nonradiometric BACTEC and Improved Oxoid Signal Blood Culture Systems in a Clinical Laboratory

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The BACTEC NR660 blood culture system, which uses infrared spectroscopy to detect carbon dioxide generated by bacterial growth, was compared with the new medium formulation of the Oxoid Signal system. Two trials were conducted: a comparative study of 88 organisms in simulated blood cultures and a clinical trial of 3,321 paired patient blood culture samples. Both trials showed that overall the BACTEC system performed better in the recovery of organisms. The Oxoid system was unable to detect by signal the growth of the majority of yeasts, nonfermentative gram-negative bacilli, *Neisseria meningitidis*, *Nocardia* spp., and *Corynebacterium jeikeium*. There were no significant differences in the yield of *Staphylococcus* spp., members of the family *Enterobacteriaceae*, *Streptococcus* spp., or anaerobic organisms. BACTEC detected growth more quickly than did the Oxoid system; 61% of the isolates were detected by BACTEC at 24 h, while 49% of the isolates were detected by Oxoid. The Oxoid system had a high proportion (58.5%) of false-positives, compared with 7.7% for the BACTEC system. Despite the new medium formulation of the Oxoid system, its performance is still not equivalent to that of the BACTEC system.

Blood for the culture of bacteria or fungi is one of the most important specimens received in a clinical microbiology laboratory. During the last 20 years, a number of blood culture systems have been developed. The initial standard was the conventional two-bottle system which requires blind subcultures and microscopic stains at timed intervals for the detection of organisms (4, 6). This is time consuming, and there is a real risk of needle stick injury during the subculturing procedures.

In the past few years, attempts have been made to improve the early recognition of microbial growth in blood cultures and to circumvent the problems with conventional systems. The BACTEC system (Johnston Laboratories, Inc., Towson, Md.) achieves this by detecting CO_2, generated by the growing organisms, either radiometrically (1) or, more recently, by infrared spectroscopy (2).

Recently, Oxoid Ltd. (Basingstoke, United Kingdom) introduced the single-bottle Signal system which detects CO_2 by simple manometry. This innovative method does not require expensive instruments to operate or the use of needles in the subculturing process. Initial evaluations (7, 9) showed the system to be inferior to the BACTEC system for the detection of certain microorganisms causing septicemia. Since then, modifications to the medium and processing methods have been made to improve the yield.

We report here the comparative performance of the improved Oxoid Signal and the nonradiometric BACTEC (NR660) blood culture systems. The evaluation was carried out in two phases: (i) an in vitro evaluation of 88 microorganisms in simulated blood cultures and (ii) a prospective comparison of 3,321 paired patient samples over a 6-month period.

MATERIALS AND METHODS

Collection of samples. For the clinical trial, 20 ml of blood was collected aseptically, when clinically indicated, from patients admitted to the Royal Adelaide Hospital. From each sample, 10 ml was inoculated into an Oxoid Signal bottle and 5 ml each was inoculated into a BACTEC NR6A (aerobic) bottle and a BACTEC NR7A (anaerobic) bottle. The volume of blood inoculated into each bottle was estimated upon arrival in the laboratory by comparison with prepared standards. Only those samples which contained a minimum of 6 ml of blood in the Oxoid bottle and 3 ml in each of the BACTEC bottles were considered adequate for inclusion in the trial.

Preparation of simulated blood cultures. Isolates used in the preparation of simulated blood cultures were obtained, when possible, from septicemic patients. The isolates consisted of members of the family *Enterobacteriaceae* (n = 8), *Pseudomonas aeruginosa* (n = 3), *Xanthomonas maltophilia* (n = 3), *Alcaligenes* species (n = 2), *Acinetobacter* species (n = 2), *Staphylococcus aureus* (n = 2), *Staphylococcus epidermidis* (n = 2), *Streptococcus pyogenes* (n = 2), viridans group streptococci (n = 6), *Streptococcus pneumoniae* (n = 6), *Haemophilus influenzae* (n = 8), *Neisseria meningitidis* (n = 3), *Clostridium perfringens* (n = 1), *Bacteroides* species (n = 8), *Fusobacterium* species (n = 4), *Peptostreptococcus anaerobius* (n = 3), *Candida albicans* (n = 3), *Candida* sp. (n = 3), *Nocardia asteroides* (n = 2), *Nocardia brasiliensis* (n = 2), *Cardiobacterium hominis* (n = 4), *Listeria monocytogenes* (n = 2), *Pasteurella multocida* (n = 2), *Eikenella corrodens* (n = 3), and *Corynebacterium jeikeium* (n = 4). Organisms were grown in broth (brain heart infusion for aerobes, thioglycolate for anaerobes) and diluted with phosphate-buffered saline for aerobes or thioglycolate broth for anaerobes to a concentration of approximately 100 CFU/ml. For each organism, 0.1 ml of this dilution was inoculated into each of the two BACTEC bottles and 0.2 ml was inoculated into the Oxoid bottle. Sterile sheep blood was then added aseptically to each BACTEC bottle (5 ml) and to the Oxoid bottle (10 ml) before incubation. The viability of each inoculum was checked by plating onto appropriate solid media. Cultures were incubated and examined by the same protocol in both the clinical and simulated trials.

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Processing of cultures. Upon receipt in the laboratory, the Oxoid Signal device was attached to the Oxoid blood culture bottle according to the instructions of the manufacturer, and the bottles were placed in a shaker-incubator at 35°C for the first 24 h and then were incubated without shaking until day 7. Oxoid bottles were inspected macroscopically twice daily for the first 2 days and then once daily until day 7. After each reading, the bottles were gently swirled before being reincubated. Gram stains and subcultures were performed when there was evidence of growth macroscopically or a positive signal. The height of the blood-broth mixture in the signal device was measured and recorded.

Both BACTEC bottles were placed on a shaker in the incubator at 35°C and incubated with shaking for the first 24 h. The aerobic (NR6A) bottles were inspected macroscopically and growth values were read twice daily for the first 2 days and then once daily until day 7. The anaerobic (NR7A) bottles were inspected macroscopically and growth values were read once daily for 7 days. Gram stains and subcultures were performed when there was evidence of growth macroscopically or when a positive growth value or significant increase in growth value was obtained. The recommendations of the BACTEC manufacturer for growth value thresholds were followed for the duration of the trial.

For the simulated trial, all bottles showing no signs of growth at 7 days were subcultured onto solid media. For the clinical trial, terminal subcultures were performed on those sets in which only one or two of the three bottles were culture positive.

Clinical assessment. All patients with positive blood cultures were assessed clinically by the clinical microbiologist as to whether the isolate from the cultures was considered to be significant or a contaminant. When this determination could not be made, the significance was designated as unknown.

Analysis of data. Statistical analysis was performed on paired data by the one-tailed Fisher's exact test.

RESULTS

Simulated trial. The results of the simulated trial of 88 organisms showed that significantly more organisms were recovered by the BACTEC system than by the Oxoid system (Table 1). A total of 13 organisms, including 3 nonfermentative gram-negative bacilli, 1 *H. influenzae* isolate, 3 *N. meningitidis* isolates, 2 *C. albicans* isolates, and 4 *Nocardia* isolates, were detected only on terminal subculture of the Oxoid system. The Oxoid system did not support the growth of four nonfermentative gram-negative bacilli and four *Corynebacterium jeikeium* isolates. Three *Peptostreptococcus anaerobius* isolates did not grow in either the BACTEC or the Oxoid system.

There were no significant differences in detection times for staphylococci, members of the family *Enterobacteriaceae*, streptococci, *P. aeruginosa*, the anaerobes, or the miscellaneous group of organisms (Table 2). The Oxoid system was significantly slower in detecting the growth of *Candida* species ($P < 0.05$) and *Cardiobacterium hominis* ($P < 0.001$) than was the BACTEC system. Growth of nonfermentative gram-negative bacilli, *Corynebacterium jeikeium*, *Nocardia* species, and *N. meningitidis* was not detected by the signal device of the Oxoid system. The cumulative yield over time (Fig. 1) indicates the superior detection rate and yield of the BACTEC system with the simulated blood cultures.

Clinical trial. A total of 3,321 blood culture sets were received during the trial. Of these, 485 (14.6%) were positive, yielding 556 isolates. The number of isolates from the BACTEC system was 434, compared with 421 from Oxoid. In the BACTEC system, the number of significant isolates causing bacteremia was 307 (70.8%), the number of contaminants was 116 (26.7%), and the significance of 11 (2.5%) isolates could not be determined. For the Oxoid system, the number of significant isolates was 296 (70.3%), the number of contaminants was 113 (26.8%), and the number of unknown significance was 12 (2.9%).

TABLE 1. Comparison of detection of growth of isolates from the BACTEC and Oxoid blood culture systems in the simulated trial

Organism group	No. of isolates			*P* value[a]
	Inoculated	Detected by:		
		BACTEC	Oxoid	
Staphylococcus spp.	4	4	4	
Enterobacteriaceae	8	8	8	
Streptococcus spp.	14	14	14	
Anaerobes[b]	16	13	13	
P. aeruginosa	3	3	3	
Nonfermentative GNB[c]	7	7	0	0.0003
Corynebacterium jeikeium	4	4	0	0.014
Nocardia spp.	4	4	0	0.014
Candida spp.	6	6	4	NS
N. meningitidis	3	3	0	NS
Cardiobacterium hominis	4	4	4	
H. influenzae	8	8	7	NS
Miscellaneous[d]	7	7	7	

[a] Calculated with Fisher's exact test. NS, Not significant. Total *P* value was 0.0001.

[b] Includes *Bacteroides* sp. ($n = 8$), *Fusobacterium* sp. ($n = 4$), *Peptostreptococcus anaerobius* ($n = 3$), and *Clostridium perfringens* ($n = 1$).

[c] GNB, Gram-negative bacilli. Includes *X. maltophilia* ($n = 3$), *Alcaligenes* sp. ($n = 2$), and *Acinetobacter* sp. ($n = 2$).

[d] Includes *Listeria* sp. ($n = 2$), *Pasteurella* sp. ($n = 2$), and *Eikenella* sp. ($n = 3$).

Of the 354 clinically significant isolates, 249 (70.3%) grew in both systems, 58 (16.4%) were detected in the BACTEC system only, and 47 (13.3%) grew only in the Oxoid system (Table 3). BACTEC was superior in the detection of yeasts ($P = 0.0007$). Of the eight yeasts isolated, only one *C. albicans* isolate grew in the Oxoid system. For all other organism groups, either there was no statistically significant difference in yield or the number of isolates was too small to compare.

Of the 249 significant isolates that grew in both systems, 193 were detected at the same time, 50 were detected more quickly by BACTEC, and 6 were detected earlier by the Oxoid system (Table 4). Staphylococci ($P = 0.0001$) and members of the family *Enterobacteriaceae* ($P = 0.0042$) were detected significantly earlier by the BACTEC system. Comparisons could not be made for other organisms because the numbers isolated were small.

The cumulative yield over time for significant isolates is shown in Fig. 2. The most significant difference between the two systems was found in the first 3 days. BACTEC detected 61, 90, and 96% of organisms on days 1, 2, and 3, respectively, compared with 49, 79, and 86% for Oxoid.

The overall contamination rates for both systems were low (BACTEC, 1.9%; Oxoid, 3.1%).

A significant difference was found between the Oxoid and BACTEC systems in the number of false-positive readings. A false-positive was defined as a positive BACTEC growth value or Oxoid Signal with no growth on subculture. A total of 58.5% of the Oxoid bottles gave false-positive readings,

TABLE 2. Speed of detection of isolates from the BACTEC and Oxoid blood culture systems in the simulated trial

Organism group[a] (no.)	Blood culture system	No. positive[b] on day:							Mean detection time (h)
		1	2	3	4	5	6	7	
Staphylococcus spp. (4)	BACTEC	4							<24
	Oxoid	4							<24
Enterobacteriaceae (8)	BACTEC	8							<24
	Oxoid	8							<24
Streptococcus spp. (14)	BACTEC	14							<24
	Oxoid	14							<24
Anaerobes (16)	BACTEC	2	9	—	—	2			54
	Oxoid	1	8	2	2	—			50
P. aeruginosa (3)	BACTEC	2	1						<24
	Oxoid	3	—						<24
Nonfermentative GNB (7)	BACTEC	1	6						36
	Oxoid	—	—	—	—	—	—	—	
Corynebacterium jeikeium (4)	BACTEC	—	1	3					61
	Oxoid	—	—	—	—	—	—	—	
Nocardia spp. (4)	BACTEC	—	4						44
	Oxoid	—	—	—	—	—	—	—	
Candida spp. (6)	BACTEC	—	4	1	—	—	1		49
	Oxoid	—	—	—	3	—	1	—	104
N. meningitidis (3)	BACTEC	—	2	1					47
	Oxoid	—	—	—	—	—	—	—	
H. influenzae (8)	BACTEC	—	4	2	2				61
	Oxoid	—	6	—	1	—	—	—	48
Cardiobacterium hominis (4)	BACTEC	—	—	4					66
	Oxoid	—	—	—	—	—	4		137
Miscellaneous (7)	BACTEC	5	1	—	1				32
	Oxoid	4	2	—	1				36

[a] For the organisms included in the anaerobes, nonfermentative gram-negative bacilli (GNB), and miscellaneous group, see Table 1, footnotes *b*, *c*, and *d*.
[b] —, No positive result given.

compared with 7.7% for the BACTEC system. The distribution of false-positives over time is shown in Table 5. The majority of the Oxoid false-positives were detected on days 3 and 4, while for the BACTEC system, most false-positives occurred on day 2.

DISCUSSION

An early report by Trombley and Anderson (7) expressed concern over the isolation of *N. meningitidis* and anaerobic organisms by the Oxoid Signal system. Modifications made to the Oxoid formulation did improve the yield of anaerobic organisms (3, 5, 8, 9), but problems still remained with the detection of *Haemophilus* species, *Neisseria* species, yeasts, and the nonfermentative gram-negative bacilli. Further modifications to the Oxoid medium to improve performance and the recent development of the nonradiometric BACTEC system provided an opportunity to compare the two improved systems for yield and mean detection time of clinically significant isolates.

This study showed no significant difference between the two systems in the recovery of staphylococci, members of the family *Enterobacteriaceae*, streptococci, and the anaer-

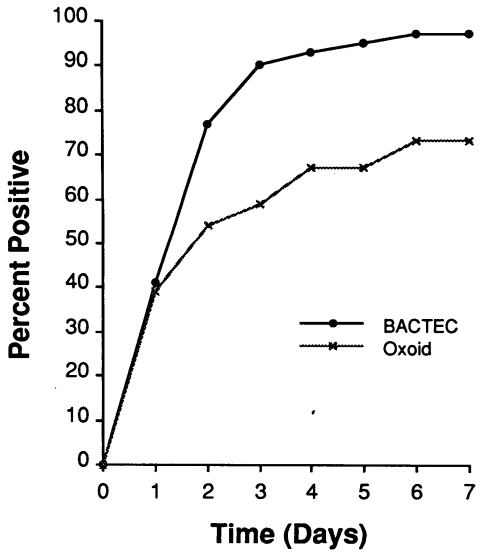

FIG. 1. Cumulative yield over time of BACTEC and Oxoid blood culture systems in the simulated trial.

TABLE 3. Comparison of yield of significant isolates from BACTEC and Oxoid blood culture systems in the clinical trial

Organism group	No. of isolates from:		
	BACTEC + Oxoid	BACTEC only	Oxoid only
Staphylococcus spp.	117	10	15
Enterobacteriaceae	61	12	17
Streptococcus spp.	43	16	8
Anaerobes[a]	7	5	4
P. aeruginosa	7	2	2
Nonfermentative GNB[b]	6	2	0
Corynebacterium sp.	2	3	0
Bacillus sp.	2	0	0
Yeasts[c]	1	7	0
N. meningitidis	1	0	0
Haemophilus spp.	0	1[d]	1[e]
Pasteurella sp.	2	0	0

[a] Includes *Bacteroides* sp., *Clostridium* sp., *Veillonella* sp., and *Peptostreptococcus* sp.
[b] GNB, Gram-negative bacilli. Includes *X. maltophilia*, *Pseudomonas* sp., *Alcaligenes* sp., and *Acinetobacter* sp.
[c] Includes *C. albicans* (n = 7) and *Cryptococcus neoformans* (n = 1).
[d] *Haemophilus parainfluenzae*.
[e] *H. influenzae*.

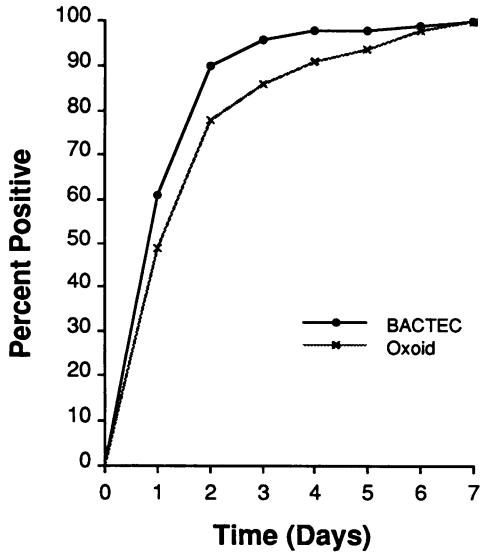

FIG. 2. Cumulative yield over time of BACTEC and Oxoid blood culture systems for clinically significant isolates.

obes. The new Oxoid medium appears to better support the growth and detection of *Haemophilus* species, which had been a problem encountered by Weinstein et al. (9), but still presents problems in the isolation of other organisms, namely *N. meningitidis*, *Candida* species, *Nocardia* species, *Corynebacterium jeikeium*, and the nonfermentative gram-negative bacilli. While the new medium is able to support the growth of some of these organisms, it is not sensitive enough to detect the growth by a positive signal, as evident in the high number of positive cultures detected only on terminal subculture during the simulated trial. This was also found in a trial by Weinstein et al. (8). The isolation of yeasts is a major concern with the Oxoid system. In this study, seven of eight episodes of septicemia due to yeasts were not detected by the Oxoid system. Further medium modifications are indicated to improve the yield of the obligate aerobes from the Oxoid system.

A comparison of the speeds of detection of significant clinical isolates showed that overall, the BACTEC system detected growth earlier than did the Oxoid system. As with other trials (8, 9), this study has shown that the greatest difference between the two systems lies in the speed of detection of the most commonly encountered isolates within the first 24 h of incubation. Although a statistical comparison could not be made for the less frequently isolated organisms, including the obligate aerobes, the trend suggests that for these isolates, BACTEC is again faster. This trend was also noted by other comparative studies (5, 8, 9). Despite the new medium formulation of the Oxoid system, it is still inferior to the BACTEC system for speed of detection of positive cultures.

The greatest problem encountered by the laboratory was the number of false-positive readings of the Oxoid system. Since the majority of false-positive Oxoid bottles gave signal heights of less than 8 mm, a modification to increase the height of the sleeve of the signal device may help to overcome the problem. This could, however, create another problem—that of not detecting true positives which give low signal heights. A total of 21 significant isolates in the clinical trial had signal heights of less than 8 mm, so growth of these isolates would not have been detected if the sleeve height were increased. High false-positive rates have also been encountered by other workers using various batches of Oxoid medium (3, 5). No explanation could be found for the high percentage of false-positives with the Oxoid system, but it seems to be related to the medium formulation.

In conclusion, this study has shown that the BACTEC NR660 blood culture system is superior to the Oxoid Signal system for both the yield and speed of detection of positive blood cultures. Further modification to improve the perfor-

TABLE 4. Comparison of speed of detection of significant isolates from BACTEC and Oxoid blood culture systems in the clinical trial

Organism group[a]	No. of isolates from:			P value[b]
	Both systems, same time	BACTEC earlier	Oxoid earlier	
Staphylococcus spp.	88	26	3	0.0001
Enterobacteriaceae	47	12	2	0.0042
Streptococcus spp.	38	4	1	
Anaerobes	5	2	0	
P. aeruginosa	7	0	0	
Nonfermentative GNB	5	1	0	
Corynebacterium sp.	0	2	0	
Bacillus sp.	1	1	0	
Yeasts	0	1	0	
N. meningitidis	0	1	0	
Pasteurella sp.	2	0	0	

[a] For organisms included in anaerobes, nonfermentative gram-negative bacilli (GNB), and yeasts, see Table 3, footnotes *a*, *b*, and *c*.
[b] Calculated by one-tailed Fisher's exact test.

TABLE 5. Distribution of false-positive readings over time in the BACTEC and Oxoid blood culture systems

System	No. of false-positives detected on day:						
	1	2	3	4	5	6	7
BACTEC	78	344	73	9	7	2	1
Oxoid	12	168	532	550	402	192	88

mance of the Oxoid system in promoting the growth of the obligate aerobes and overcoming the problem of false-positive signals would enable the system to be more attractive. Terminal subculturing of the Oxoid system would increase the yield of the strict aerobes. While the Oxoid system is very easy to use in the laboratory, does not involve the use of expensive equipment, and allows cultures to be read as required, its performance is still not equivalent to that of the BACTEC system.

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LITERATURE CITED

1. **DeLand, F. H., and H. N. Wagner, Jr.** 1969. Early detection of bacterial growth with carbon-14-labelled glucose. Radiology **92:** 154–155.
2. **Jungkind, D., J. Millan, S. Allen, J. Dyke, and E. Hill.** 1986. Clinical comparison of a new automated infrared blood culture system with the BACTEC 460 system. J. Clin. Microbiol. **23:** 262–266.
3. **Murray, P. R., A. C. Niles, R. L. Heeren, M. M. Curren, L. E. James, and J. E. Hoppe-Bauer.** 1988. Comparative evaluation of the Oxoid Signal and Roche Septi-Chek blood culture systems. J. Clin. Microbiol. **26:**2526–2530.
4. **Reller, L. B., P. R. Murray, and J. D. MacLowery.** 1982. Cumitech 1A, Blood cultures II. Coordinating ed., J. A. Washington II. American Society for Microbiology, Washington, D.C.
5. **Rimmer, K., and M. Cabot.** 1988. Comparison of Bactec NR-660 and Signal systems. J. Clin. Pathol. **41:**676–678.
6. **Silva, H. S., and J. A. Washington II.** 1980. Optimal time for routine early subculture of blood cultures. J. Clin. Microbiol. **12:**445–446.
7. **Trombley, C., and J. D. Anderson.** 1987. Signal blood culture system for detection of bacteremia in neonates. J. Clin. Microbiol. **25:**2098–2101.
8. **Weinstein, M. P., S. Mirrett, L. G. Reimer, and L. B. Reller.** 1989. Effect of agitation and terminal subcultures on yield and speed of detection of the Oxoid Signal blood culture system versus the BACTEC radiometric system. J. Clin. Microbiol. **27:**427–430.
9. **Weinstein, M. P., S. Mirrett, and L. B. Reller.** 1988. Comparative evaluation of Oxoid Signal and BACTEC radiometric blood culture systems for the detection of bacteremia and fungemia. J. Clin. Microbiol. **26:**962–964.