

Evaluation of the BACTEC Antimicrobial Removal System for Detection of Bacteremia

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The BACTEC 16B resin medium was developed to detect bacteremia in patients receiving antimicrobial therapy. Over a 9-month period, we compared the efficacy of the BACTEC 16B bottle to the conventional aerobic BACTEC 6B bottle. Of a total of 1,524 sets of blood cultures, 79 yielded presumed pathogens. Of these 79 sets, 42 (53.2%) were positive in both the 16B and 6B bottles, 23 (29.1%) were positive only in the 16B bottle, and 14 (17.7%) were positive only in the 6B bottle. For patients receiving antimicrobial drugs, 33 of 34 (97.1%) sets were positive for pathogens in the 16B bottle, but only 15 of 34 (44.1%) were positive in the 6B bottle. In 19 (55.9%) of the 34 sets, only the 16B bottle yielded growth. The resin bottle was more useful for patients with gram-positive bacteremia than for those with gram-negative bacteremia. The BACTEC 16B resin medium increases the recovery of organisms from bacteremic patients receiving antimicrobial agents and should be used in addition to the standard BACTEC aerobic bottle for such patients.

Early identification and antimicrobial susceptibility testing of organisms causing bacteremia are high priorities in clinical microbiology laboratories. Many patients may receive antimicrobial agents before blood cultures are taken, which causes delay in recovering the organisms from conventional blood culture media. Recently, systems employing cationic and polymeric adsorbent resins to remove antimicrobial agents from blood have been developed (1, 2, 4, 9, 10). The most data have accumulated for the antibiotic removal device (ARD) (Marion Scientific, Kansas City, Mo.), which is used before blood is cultured in standard media. The effectiveness of the ARD in enhancing the yield of blood cultures was excellent in some studies (2, 9) and equivocal in others (10).

A similar ARD is now available for BACTEC, the automated radiometric system for detecting bacterial growth (Johnston Laboratories, Cockeysville, Md.). The BACTEC 16B tryptic soy broth system consists of an aerobic bottle with adsorbent resins, similar to the ARD in principle. To date, only one study has been reported on the usefulness of the BACTEC 16B medium in increasing the yield of positive cultures for patients on antimicrobial therapy (1).

The purposes of this study were to determine whether the BACTEC 16B medium was more effective than conventional blood culturing tech-

niques in recovering organisms from the blood of patients on antimicrobial therapy and whether the 16B medium with resins could replace the standard aerobic bottle used in the BACTEC system.

MATERIALS AND METHODS

Patients. Between January and September 1982, all patients at the Ann Arbor Veterans Administration Medical Center for whom blood cultures were taken were eligible for this study. Physicians were encouraged to use the BACTEC 16B bottle in addition to the conventional aerobic and anaerobic BACTEC bottles for blood cultures for all patients with suspected bacteremia regardless of whether antimicrobial therapy had been started. All patients whose blood was cultured in the 16B bottle were included in the study. Those patients with positive blood cultures in the 6B or 16B bottle were seen by the infectious diseases service.

Collection and processing of specimens. Blood was drawn aseptically by the house staff at the bedside of the patient. Three to five milliliters of blood was inoculated into each of three bottles: the aerobic BACTEC 6B, containing 30 ml of tryptic soy broth with 0.025% sodium polyanethol sulfonate; the anaerobic BACTEC 7C, containing 30 ml of preduced, anaerobically sterilized tryptic soy broth with 0.025% sodium polyanethol sulfonate; and the aerobic BACTEC 16B, containing 30 ml of tryptic soy broth with 0.025% sodium polyanethol sulfonate and both a non-ionic adsorbent resin and a cationic exchange resin for

TABLE 1. Comparison of BACTEC 16B medium (with resins) with conventional BACTEC 6B medium

BACTEC medium	No. of sets ^a positive for:	
	Contaminants	Pathogens
16B	2 (2)	23 (19)
6B	9 (2)	14 (1)
16B and 6B	4 (1)	42 (14)

^a The number of sets from patients who received prior antimicrobial therapy is shown in parentheses.

antimicrobial agent removal. The aerobic 6B and 16B bottles were shaken at 35°C for 48 h; the anaerobic bottle was not agitated. Bottles were held for a total of 7 days at 35°C.

Detection of positive cultures. All bottles were checked daily for 7 days for radioisotope utilization on a BACTEC 460 (Johnston Laboratories). Cultures with growth index values exceeding the threshold units (a growth index of ≥ 30 for 6B, ≥ 20 for 16B, and ≥ 10 for 7C) and those positive by visual examination (showing hemolysis, turbidity, or bulging septum) were immediately Gram stained and subcultured onto Trypticase soy agar with 5% sheep blood, chocolate GC agar, and MacConkey agar (BBL Microbiology Systems, Cockeysville, Md.).

RESULTS

Over the 9-month study period, 2,414 blood culture sets were drawn. Of this number, 1,524 sets included the 16B resin bottle. Of these 1,524 sets, 94 (6.2%) from 57 different patients yielded

growth (Table 1). Of the 94, 15 (16%) were judged to contain contaminants; the organisms isolated included *Staphylococcus epidermidis* (10 sets), diphtheroids (2 sets), *Bacillus* species (2 sets), and *Streptococcus mitis* (1 set). Nine of these 15 appeared only in the conventional 6B medium.

Of the 94 sets, 79 (84%) yielded presumed pathogens. Of this number, 42 (53.2%) were positive in both the conventional and the 16B resin media, 23 (29.1%) were positive only in the 16B resin medium, and 14 (17.7%) were positive only in the conventional medium. Thus, in 65 sets the 16B bottle was positive, and in 56 sets the 6B bottle was positive ($P < 0.1$, chi-square test).

All of the pathogenic organisms cultured, including *Candida* species, were represented in both bottles, although the BACTEC 16B appeared to be the most useful for patients with gram-positive bacteremia (Table 2). Of the 34 sets of blood cultures positive for pathogens from patients receiving antimicrobial therapy, the 16B medium was positive for 33 (97.1%) and the 6B medium was positive for 15 (44.1%) ($P < 0.0005$, chi-square test). The 16B medium was the only one positive for 19 of the 34 (55.9%), but the 6B medium was the only one positive in only one instance (2.9%). Of the 19 sets which were positive only in the 16B bottle, 16 (84.2%) yielded gram-positive cocci, 15 of which were staphylococci. In all but three instances, gram-

TABLE 2. Pathogenic organisms isolated in BACTEC 16B and BACTEC 6B media^a

Organism	No. of sets ^b positive in BACTEC medium:		
	16B only	6B and 16B	6B only
Gram positive			
<i>Staphylococcus aureus</i>	11 (10)	8 (1)	4
<i>Staphylococcus epidermidis</i>	5 (5)	6 (2)	1
Viridans streptococci		2	
<i>Streptococcus faecalis</i>	1 (1)	1 (1)	
<i>Streptococcus pneumoniae</i>		2	
<i>Listeria monocytogenes</i>		4	
Gram negative			
<i>Escherichia coli</i>	3 (3)	4 (2)	2
<i>Klebsiella pneumoniae</i> - <i>Klebsiella oxytoca</i>		6 (2)	1
<i>Pseudomonas aeruginosa</i>		7 (2)	2 (1)
<i>Serratia marcescens</i> / <i>Serratia liquefaciens</i>		2 (2)	1
<i>Enterobacter cloacae</i> / <i>Enterobacter agglomerans</i>		3 (1)	
<i>Acinetobacter calcoaceticus</i>		1 (1)	
Fungi			
<i>Candida albicans</i> - <i>Candida parapsilosis</i>	2	1	3

^a Several patients had polymicrobial bacteremia. Contaminants are not included.

^b The number of sets from patients who received prior antimicrobial therapy is shown in parentheses.

negative bacteremia was documented by growth in both the 6B and 16B bottles.

The time until detection of bacteremia was the same for 38 of the 42 sets that were positive in both bottles. In three sets the 16B medium yielded growth 24 to 36 h sooner than the 6B medium, and in one set the 6B medium was positive 6 h before the 16B medium.

DISCUSSION

Prior antimicrobial therapy may contribute to the failure to recover microorganisms from blood cultures taken from bacteremic patients. To improve the detection of microorganisms in the presence of antimicrobial agents, several modifications of the techniques for obtaining blood cultures have been made. The simplest, that of diluting the blood 10-fold, often reduces the concentration of antibiotics below inhibitory levels (6).

Penicillinase may be added to blood culture media to inactivate β -lactam antibiotics (8). However, because of well-documented instances of contaminated penicillinase (3, 5), most laboratories do not add this substance to the blood culture media. Sodium polyanethol sulfonate, a polyanionic anticoagulant which is both antiphagocytic and anticomplementary, inhibits the aminoglycoside antibiotics (8). It has been shown to increase the recovery of bacteria from blood cultures (7) and is routinely added to most commercially available blood culture media.

The ARD was developed as another approach to the problem of removing antimicrobial agents (4, 9). Appleman et al. (2) found that using the ARD increased the detection rate and decreased the time required to detect bacteremia in patients receiving concomitant antimicrobial therapy. However, Wright et al. (10) found that the ARD improved neither the isolation rate nor the time to positivity compared with conventional blood culture techniques. The main drawback of the ARD is that the specimen must be inoculated into the resin bottle and shaken for 15 min before it can be transferred to the routine blood culture medium. The ARD technique may cause hemolysis and turbidity, making it difficult to visually assess the culture bottle. In addition, the ARD is expensive in terms of technician time; for small laboratories without adequate nighttime staff, the ARD is impractical.

Recently, a resin medium was designed for use with the BACTEC radiometric device. A collaborative study concluded that this technique significantly improved both the detection rate and the time to positivity for blood cultures obtained from patients receiving antimicrobial agents (1). Our data confirmed that the BAC-

TEC 16B medium increased the detection rate of bacteremia in patients receiving antimicrobial therapy compared with the standard BACTEC 6B medium. The resin bottle was clearly most effective for patients with gram-positive bacteremia. Although this could be caused by more effective inactivation of β -lactam-type antibiotics by the resin, it seems more likely that gram-positive cocci are more easily inhibited by appropriate antimicrobial agents than are gram-negative bacilli. Thus, even in the presence of antibiotics, the gram-negative bacilli were able to grow in the 6B bottle. Use of the 16B bottle did not increase the contamination rate; in fact, contaminants were isolated more often from the 6B bottle. The reason for this is not clear.

Although the 16B bottle appeared to support the growth of all pathogens isolated in this study, we do not believe that it could replace the 6B bottle. In 14 sets, the 6B bottle alone was positive; this occurred for patients with gram-positive and gram-negative bacteremia, as well as fungemia. The 16B bottle should be readily available for use with the 6B bottle for hospitalized patients who become septic while receiving antimicrobial therapy and for those patients, such as intravenous drug abusers or those transferred from other hospitals, who are likely to have received antibiotics before admission to the hospital.

LITERATURE CITED

1. Applebaum, P. C., D. G. Beckwith, J. R. Dipersio, J. W. Dyke, J. F. Salventi, and L. L. Stone. 1983. Enhanced detection of bacteremia with a new BACTEC resin blood culture medium. *J. Clin. Microbiol.* 17:48-51.
2. Appleman, M. D., R. S. Swinney, and P. N. R. Heseltine. 1982. Evaluation of the antibiotic removal device. *J. Clin. Microbiol.* 15:278-281.
3. Faris, H. M., Jr., and F. F. Sparling. 1972. *Mima polymorpha* bacteremia: false-positive cultures due to contaminated penicillinase. *J. Am. Med. Assoc.* 219:76-77.
4. Lindsey, N. J., and P. E. Riely. 1981. In vitro antibiotic removal and bacterial recovery from blood with an antibiotic removal device. *J. Clin. Microbiol.* 13:503-507.
5. Norden, C. W. 1969. Pseudosepticemia. *Ann. Intern. Med.* 71:789-790.
6. Reller, L. B., P. R. Murray, and J. D. MacLowry. 1982. Cumitech 1A, Blood cultures II. Coordinating ed., J. A. Washington II. American Society for Microbiology, Washington, D.C.
7. Rosner, R. 1968. Effect of various anticoagulants and no anticoagulant on ability to isolate bacteria directly from parallel clinical blood specimens. *Am. J. Clin. Pathol.* 49:216-219.
8. Tilton, R. C. 1982. The laboratory approach to the detection of bacteremia. *Annu. Rev. Microbiol.* 36:467-493.
9. Wallis, C., J. L. Melnick, R. D. Wende, and P. E. Riely. 1980. Rapid isolation of bacteria from septicemic patients by use of an antimicrobial agent removal device. *J. Clin. Microbiol.* 11:462-464.
10. Wright, A. J., R. L. Thompson, C. A. McLimans, W. R. Wilson, and J. A. Washington II. 1982. The antimicrobial removal device: a microbiological and clinical evaluation. *Am. J. Clin. Pathol.* 78:173-177.