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Yield, Clinical Significance, and Cost of a Combination BACTEC plus Septi-Chek Blood Culture System

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A blood culture was performed by adding a vented Septi-Chek bottle (Roche Diagnostics, Div. Hoffmann-LaRoche Inc., Nutley, N.J.) to a standard BACTEC system (Johnston Laboratories, Inc., Towson, Md.) blood culture. The yield of bacteremic patients, the clinical significance of organisms detected, and the cost of the combination system were compared with those of the standard BACTEC system alone. Each culture included 20 ml of blood divided among a BACTEC 6B aerobic bottle (5 ml), a BACTEC 7D anaerobic bottle (5 ml), and a Septi-Chek bottle equipped with a slide subculture attachment (10 ml). Significant isolates grew in 9.6% of the 2,269 cultures evaluated. The combination BACTEC plus Septi-Chek system detected 25% more bacteremic patients than the BACTEC system alone, 129 patients versus 103. The 26 bacteremic patients detected by only the added Septi-Chek bottle included 7 whose organism was isolated from blood alone and 19 whose organism was in mixed or pure culture from a second source. Detection of the organism resulted in alteration of antimicrobial therapy in 17 of these 26 patients. The combination system, which cultured a 20-ml blood volume, cost $11,000 more during the study period than the BACTEC system alone, which cultured a 10-ml volume. Reimbursement under the diagnosis-related group system was increased by $23,000 as a result of documentation of sepsis in these 26 patients. Blood volume and, possibly, the use of multiple blood culture systems are important factors when selecting a blood culture procedure for routine use.

A blood culture represents one of the most important diagnostic tests a clinical microbiology laboratory performs. An ideal blood culture should detect the maximum number of bacteremic patients at a minimum cost. To improve sensitivity, investigators have advocated increasing the volume of blood cultured and combining blood culture systems (6, 7).

Ilstrup and Washington (4), using a conventional blood culture system, showed 36% more isolates when the volume of blood per culture was increased from 10 to 20 ml. Plorde and collaborators (5), using the BACTEC radiometric blood culture system, demonstrated a 15% increase in positive cultures when a 20-ml blood volume culture was compared with a 10-ml volume culture. In spite of these findings, a recent survey of blood culture methods reported that 63% of 288 laboratories which responded collected 10 ml or less blood per culture and that only 16% collected more than 15 ml per culture (K. S. Kehl, Clin. Microbiol. Newsl. 8:117–123, 1986).

A review of new approaches to blood cultures (7) suggested that a combination of blood culture systems allows the advantages of one system to offset the disadvantages of the other. As an example, the Isolator system (E. I. du Pont de Nemours & Co., Inc., Wilmington, Del.) detected significantly more members of the family *Enterobacteriaceae*, staphylococci, and yeasts but significantly fewer *Pseudomonas* spp., streptococci, and anaerobes than did the BACTEC system (1). Use of these two systems together would ensure improved recovery of a wide range of microorganisms.

The value of combining blood culture systems and culturing larger volumes of blood can be examined by reviewing publications which compared systems. Weinstein et al. (8) compared the BACTEC and Septi-Chek systems. Overall, both systems were comparable. However, both systems combined detected approximately 20% more organisms than either system used by itself. A combined blood culture system culturing larger volumes of blood does increase the yield of microorganisms. In contrast to modifications which improve the yield of a blood culture system, the importance of containing laboratory expenses may prevent the use of a better system which would increase costs prohibitively. With both improved detection and cost containment in mind, we examined the yield of bacteremic patients, clinical significance of detecting additional organisms, and cost of a combination BACTEC plus Septi-Chek blood culture system.

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MATERIALS AND METHODS

Twenty milliliters of blood for culture was collected by venipuncture after antisepsis with povidone-iodine. The protocol for the number and timing of cultures per patient included a minimum of two and a maximum of three cultures each day. When antimicrobial agents were to be started immediately, two cultures, generally spaced no more than 10 min apart, were drawn before infusion of drugs. When antimicrobial agents were not to be started immediately, three cultures were drawn over an 8- to 24-h period, spaced at least 1 h apart.

Each 20-ml sample was divided into a BACTEC 6B aerobic bottle (Johnston Laboratories, Inc., Townson, Md.) (5 ml), a BACTEC 7D anaerobic bottle (5 ml), and a Septi-Chek (Roche Diagnostics, Div. Hoffmann-LaRoche Inc., Nutley, N.J.) bottle with Trypticase soy broth (BBL Microbiology Systems, Cockeysville, Md.) equipped with a slide subculture attachment (10 ml). The BACTEC 6B bottle

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TABLE 1. Bacteremic patients detected by a standard BACTEC system culture and a combination BACTEC plus Septi-Chek system culture[a]

Organism(s)	No. of bacteremic patients detected by:	
	Standard BACTEC system (10-ml blood volume)	Combination BACTEC plus Septi-Chek system (20-ml blood volume)[b]
Enterobacteriaceae		
Citrobacter freundii	0	1
Escherichia coli	27	34
Klebsiella pneumoniae	5	8
Proteus vulgaris	0	1
Serratia marcescens	2	3
Other	11	11
Gram-negative non-*Enterobacteriaceae*		
Pseudomonas aeruginosa	2	4
Other	4	4
Staphylococci		
Staphylococcus aureus	8	13
Staphylococcus sp. (coagulase negative)	1	1
Streptococci		
Streptococcus agalactiae	2	2
Enterococcus sp.	8	8
Viridans group streptococci	3	3
Streptococcus pneumoniae	7	7
Other gram-positive organisms		
Listeria monocytogenes	1	1
Anaerobes	3	3
Yeasts	2	4
Mixed organisms	17	21
Total	103	129

[a] A standard BACTEC system culture included both 6B aerobic and 7D anaerobic bottles, each inoculated with 5 ml of blood. The combination system included these two bottles with a Septi-Chek bottle added. The Septi-Chek bottle was inoculated with 10 ml of blood and equipped with a slide subculture attachment.

[b] Organisms detected by the combination system but not by the standard BACTEC system were detected in the Septi-Chek bottle only.

was placed on a shaker for 24 h. All cultures were incubated at 35 to 37°C. BACTEC cultures were radiometrically checked twice daily on days 1 and 2 and once daily on days 3 through 7. Septi-Chek bottles were subcultured by inversion upon receipt in the laboratory, again 3 to 16 h later, and thereafter once daily through day 7.

The BACTEC 6B and 7D bottles were considered the standard BACTEC system culture. The combination system included these two bottles plus the Septi-Chek bottle. The total blood volume per culture was 10 ml for the BACTEC system and 20 ml for the combination system.

A patient's bacteremic episode, including fungemia, was defined by the first positive blood culture or by a new positive culture occurring more than 7 days after the preceding positive culture. Any positive culture obtained within 1 week of a previous positive culture was considered to represent the same episode.

The following organisms were considered contaminants unless multiple culture sets were positive or review of other laboratory and clinical information indicated that the organisms were clinically significant: *Staphylococcus epidermidis*, *Corynebacterium* spp., *Propionibacterium* spp., *Lactobacillus* spp., *Bacillus* spp., and saprophytic *Neisseria* spp. Contaminants were not counted and analyzed in this study.

Cost of materials was calculated by using volume discounts available to our hospital. All expendable materials, except those needed for phlebotomy, and service contracts were included. The cost for purchase of the BACTEC 460 instrument, data recorder, and shaker was not included. Unit values for labor were 5.0 min per bottle for the BACTEC system and 5.0 min per bottle for the Septi-Chek system. The average hourly wage used was $12.63, which included fringe benefits.

Charts were reviewed by an infectious-disease physician (T.M.F.). Antimicrobial therapy was considered altered if specific treatment, including choice of antimicrobial agent or length of therapy, was chosen because of the blood isolate and accompanying antimicrobial susceptibility tests.

Diagnosis-related group (DRG) reimbursement was calculated by using Code 3-3M software codefinder based on Health Care Financing Administration weights (3). Akron City Hospital is rated as an acute-care facility with an approved teaching program for determination of the blended target rate. Reimbursement for all patients was based on Medicare values.

RESULTS

Overall, 2,269 cultures were evaluated during a 5-month period. There were 276 positive cultures, of which 217 (9.6%) contained significant isolates and 59 (2.6%) contained contaminants.

The 10-ml blood volume cultured with the standard BACTEC system compared with the 20-ml blood volume cultured with the combination system detected 205 versus 250 organisms, 177 versus 217 positive cultures, and 103 versus 129 bacteremic patients, respectively. The increases in yields of organisms, positive cultures, and bacteremic patients with the combination system were 22, 23, and 25%, respectively.

The organisms isolated from all 129 bacteremic patients are listed in Table 1. Of these patients 26 were detected by the combination system but missed by the standard BACTEC system, indicating detection by growth in the Septi-Chek bottle only. The clinical significance of detecting organisms in these patients is represented by the facts that in 7 of the 26 patients the etiologic agent was isolated from blood only and in 11 of 26 patients the etiologic agent was isolated from blood and in mixed culture from a primary site. In the remaining eight patients, the etiologic agent was isolated from blood and in pure culture from a primary site. Antimicrobial therapy was altered because of the positive blood culture report in 17 of the 26 patients (Table 2). Of the nine bacteremic patients for whom antimicrobial therapy was not altered because of the blood isolate, one had a presumed transient *Staphylococcus aureus* bacteremia and was not treated. Another had peritonitis caused by a mixture of facultative and anaerobic bacteria, and therapy did not need to be altered after the report of *Fusobacterium* sp. isolated from the blood. Seven had pyelonephritis in which the same organism was isolated from urine and blood. Each of these patients was considered septic clinically, and anti-

TABLE 2. Clinical significance of detecting additional bacteremic patients by using a combination BACTEC plus Septi-Chek blood culture system[a]

Organism isolated from:	Age (yr)/sex	Primary site of infection[b]	Blood isolate	Antimicrobial therapy altered because of positive blood culture
Blood only	69/Male	?	*Staphylococcus aureus*	Yes
	77/Male	? Intestinal	*Escherichia coli*	Yes
	74/Male	? Respiratory	*Pseudomonas putida*	Yes
	85/Male	? Urinary	*Enterococcus* sp.	Yes
	68/Female	? Urinary	*Staphylococcus aureus*	Yes
	50/Male	? Respiratory	*Staphylococcus aureus*	No
	50/Male	? Respiratory	*Klebsiella pneumoniae*	Yes
Blood and in mixed culture from a primary site	73/Male	Ileostomy	*Escherichia coli*	Yes
	72/Female	Urinary	*Escherichia coli*	Yes
	77/Male	Respiratory	*Serratia marcescens*	Yes
	68/Male	Wound	*Candida parapsilosis*	Yes
	44/Male	Respiratory	*Staphylococcus aureus*	Yes
	56/Male	Bone (foot)	*Proteus vulgaris*	Yes
	66/Male	Urinary	*Klebsiella pneumoniae*	Yes
	59/Male	Urinary	*Escherichia coli*	Yes
	23/Male	Respiratory	*Pseudomonas aeruginosa*	Yes
	35/Female	Wound	*Torulopsis glabrata*	Yes
	85/Female	Peritoneum	*Fusobacterium* sp.	No
Blood and in pure culture from a primary site	80/Female	Urinary	*Escherichia coli*	No
	82/Female	Urinary	*Pseudomonas aeruginosa*	No
	80/Male	Respiratory	*Staphylococcus aureus*	Yes
	87/Male	Urinary	*Escherichia coli*	No
	20/Female	Urinary	*Citrobacter freundii*	No
	64/Female	Urinary	*Klebsiella pneumoniae*	No
	52/Female	Urinary	*Escherichia coli*	No
	22/Female	Urinary	*Escherichia coli*	No

[a] Twenty-six of 129 bacteremic patients whose organisms were detected by the Septi-Chek bottle only when a combination BACTEC plus Septi-Chek blood culture system was used.
[b] ?, Primary site of infection unknown or questionable.

microbial therapy was already determined to be necessary for upper tract infection before notification of the positive blood culture.

The material and labor costs of a standard BACTEC system culture and a combination BACTEC plus Septi-Chek system culture were $5.34 and $10.14, respectively. The combination system cost $10,892 more during the 5-month study period than did the standard BACTEC system. For comparative purposes, a 20-ml blood volume cultured with four BACTEC bottles would have cost $10.68, and using two Septi-Check bottles, one vented with a slide subculture attachment and one nonvented, would have cost $7.10. The former would have cost $12,117 more, and the latter would have cost $3,994 more during the study period than would the standard BACTEC system culture (Table 3).

The hospital DRG reimbursement is sometimes changed when a clinical impression of sepsis is documented by isolation of an organism from the blood. Reimbursement for 9 of the 26 bacteremic patients, detected by the combination culture but not the standard BACTEC culture, was increased a total of $23,246 (Table 4).

TABLE 3. Cost of BACTEC and Septi-Chek blood culture system or system combination

System or combination	Blood vol (ml)	Cost ($)/culture			Cost ($) per study period (2,269 cultures)
		Materials	Labor	Total	
BACTEC (2 bottles)[a]	10	3.24	2.10	5.34	12,116
BACTEC (2 bottles) + Septi-Chek (1 bottle)[b]	20	6.99	3.15	10.14	23,008

[a] Bottles, 6B aerobic and 7D anaerobic.
[b] Bottles, 6B aerobic and 7D anaerobic; vented Trypticase soy broth with a slide subculture attachment was included.

TABLE 4. DRG reimbursement increase as a result of detecting additional bacteremic patients with a combination BACTEC plus Septi-Chek blood culture system[a]

Patient no. and primary diagnosis[b]	DRG reimbursement ($)		Increased reimbursement because of positive blood cultures ($)
	Without positive blood cultures	With positive blood cultures	
1 UTI with sepsis	2,140	4,877	2,737
2 UTI with sepsis	2,555	4,877	2,322
3 UTI with sepsis	2,140	4,877	2,737
4 Cholangitis with sepsis	2,671	4,877	2,206
5 UTI with sepsis	2,555	4,877	2,322
6 UTI with sepsis and gallstones	3,469	5,657	2,188
7 UTI with sepsis	2,140	4,877	2,737
8 UTI with sepsis	2,555	4,877	2,322
9 UTI with sepsis	1,202	4,877	3,675
Total	21,427	44,673	23,246

[a] Increased reimbursement for 9 of 26 bacteremic patients whose organism was detected by the Septi-Chek bottle only when a combination BACTEC plus Septi-Chek blood culture system was used.
[b] UTI, Urinary tract infection.

DISCUSSION

By adding a vented Septi-Chek bottle to a standard BACTEC system blood culture, we demonstrated that a 20-ml blood volume cultured with a combination BACTEC plus Septi-Chek system yielded more organisms, positive cultures, and bacteremic patients than did a 10-ml volume cultured with the standard BACTEC system alone. Specifically, the combination system detected 25% more bacteremic patients than did the BACTEC system (Table 1). All patients had a minimum of either two or three blood cultures. If one counts the total blood volume cultured per patient, the combination system cultured 40- or 60-ml blood volumes and the standard BACTEC system cultured 20- or 30-ml volumes. For a bacteremic patient to be detected by the combination system only, the isolate was detected in the Septi-Chek bottle, and all BACTEC system bottles inoculated within 1 week of the original bacteremic episode failed to grow the etiologic agent.

Whether the improved yield of isolates, positive cultures, and bacteremic patients was a result of the additional blood volume or the use of two separate systems was not resolved by our study. Based on a recent publication (8) comparing the BACTEC and Septi-Chek systems, which concluded that there were only minor differences between the two systems, volume of blood cultured may be more important. However, in that study each system did have advantages. Significantly more *Enterobacteriaceae* were detected by the Septi-Chek system. The BACTEC system detected more anaerobic bacteria and the Septi-Chek system detected more fungi, but small numbers of recovered organisms precluded statistical significance. In our study, if the Septi-Chek bottle had been considered the standard system, addition of two BACTEC bottles would have improved the yield of isolates by 22%. Although this increase is identical to that seen when the Septi-Chek bottle was added to the standard BACTEC system, differences in systems do exist. We too discovered that Septi-Chek detected more *Enterobacteriaceae* and BACTEC detected more anaerobes.

The combination system increased detection of bacteremia regardless of etiology, with the exception of the streptococci (Table 1). Commonly detected organisms, such as *Escherichia coli*, *Klebsiella pneumoniae*, and *S. aureus*, were all detected more frequently by the combination system. The streptococci isolated from 20 patients were, however, all detected by the standard BACTEC system. We speculate that the quantities of bacteria per volume of blood for the streptococci were sufficiently high to allow detection by the smaller blood volume system.

To determine the clinical significance of detecting the 26 additional bacteremic patients with the combination system, we reviewed the charts of patient to determine sites of isolation of the infectious agent and whether the positive blood culture report necessitated alteration of antimicrobial therapy (Table 2). In 7 of the 26 patients, the etiologic agent of infection was isolated from blood only. In six of these patients, antimicrobial therapy was altered after a positive blood culture report. One patient with *S. aureus* isolated from the blood did not require therapy. In 11 of 26 patients, the microorganism was isolated from the blood and in mixed culture from the primary site of infection. Most primary sites were subject to contamination by normal flora, and a definitive role in the infection process for an isolate was difficult to determine. The positive blood culture established the importance of one of the isolates and did lead to alteration of antimicrobial therapy in 10 of the 11 patients. Information from a positive blood culture report was least helpful with those patients whose infectious agent was isolated from blood and in pure culture from the primary site of infection. Of the eight patients in this group, seven had urinary tract infection and none required alteration of antimicrobial therapy. The eighth patient had *S. aureus* pneumonia, and therapy was lengthened because of the positive blood culture. Overall, 17 of the 26 patients had their antimicrobial therapy altered because of blood culture information.

Use of a combination BACTEC plus Septi-Chek blood culture system nearly doubled the total cost of performing a culture (Table 3). The cost during the 5-month study period for performing 2,269 cultures rose from $12,116 for the standard BACTEC system to $23,008 for the combination system. Assuming that blood volume is the most important factor contributing to increased yield, the cost for other 20-ml culture systems was tabulated. As suggested by Plorde et al. (5), four BACTEC bottles could be used to culture a 20-ml blood volume. This approach is costly, $10.68 per culture or $24,233 during our study period. In our laboratory, doubling the number of BACTEC bottles from two to four per culture would necessitate acquiring a second BACTEC instrument. If the approach of Colmer and Sodeman (2), dividing 20 ml of blood among three BACTEC bottles, were used, the cost would be $8.01 per culture or $18,175 during the study period. The latter approach, however, leads to insufficient dilution of blood in culture broth. A two-bottle Septi-Chek system is the least expensive approach, costing $7.10 per culture or $16,110 for the study period. This amounts to $3,994 more during the study period than with the standard BACTEC system culture.

DRG reimbursement was increased for 9 of the 26 bacteremic patients detected by the combination system only. The total increase amounted to $23,246 (Table 4). Reimbursement was calculated by assuming that all 26 patients were Medicare patients. In truth, approximately 50% of our hospitalized patients are currently included in a DRG reimbursement program. This percentage is increasing. Theoretically, the additional $23,246 generated offsets the increased expense of culturing a larger volume of blood with or without the use of a second blood culture system. Interestingly, reimbursement was increased for those patients whose positive blood culture information was least likely to alter antimicrobial therapy.

In summary, adding a Septi-Chek bottle to a standard BACTEC system blood culture increased the number of bacteremic patients detected by 25%. The positive blood culture information was felt to be clinically useful for 17 of the 26 bacteremic patients detected by the combination system only, as measured by alteration of antimicrobial therapy. The increased cost associated with culturing larger volumes of blood may be offset by an increase in DRG reimbursement associated with documentation of sepsis. Optimally, a 20-ml blood volume should be cultured by a combination BACTEC plus Septi-Chek system. However, a reasonable compromise might include using four BACTEC bottles or two Septi-Chek bottles.

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