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Clinical Comparison of Isolator and Thiol Broth with ESP Aerobic and Anaerobic Bottles for Recovery of Pathogens from Blood

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The recovery of pathogens and the speed of their detection were determined for our conventional blood culture system (an Isolator [Wampole] and a 100-ml Thiol bottle [Difco]) compared with automated ESP aerobic and anaerobic bottles (80 ml each; Difco). Each of the four culture devices was inoculated with approximately 10 ml of blood from symptomatic patients weighing more than 80 lb (ca. 36 kg). From 7,070 sets of cultures for 2,841 patients, 607 clinically significant isolates were recovered: 456 (75.1%) from the Isolator, 353 (58.2%) from Thiol, 377 (62.1%) from ESP aerobic bottles, and 346 (57.0%) from ESP anaerobic bottles. Of the 607 isolates, 149 (24.5%) were detected only with the conventional system (Isolator and/or Thiol), and 65 (10.7%) were detected only with the ESP two-bottle system ($P < 0.001$). Our conventional system allowed for detection of significantly more isolates of members of the family *Enterobacteriaceae* ($P < 0.001$), *Staphylococcus aureus* ($P < 0.01$), *Staphylococcus* spp. (coagulase-negative) ($P < 0.01$), and *Enterococcus* spp. ($P < 0.05$), and ESP facilitated detection of significantly more isolates of *S. pneumoniae* ($P < 0.01$). When all four devices in a culture set were positive for the same isolate, no microbial species or group was detected significantly earlier (≥24 h) by either blood culture system. The Isolator contamination rate (4.8%) was ≥6 times the rate for any of the bottles. Of pathogens detected by the Isolator, 50% were recovered in counts of ≤1.0 CFU/ml and 18% were recovered only as a single colony. The ESP system offered an automated, less labor-intensive blood culture system for which routine subcultures were not required, but the important considerations of culturing large volumes of blood and of obtaining at least two sets from each patient in our population were reemphasized.

An increasing number of automated systems for detection of microbial pathogens in patients' blood samples are now either commercially available or under development. Among the many important factors in the selection of one of these systems for routine use are both the volume of broth contained within the bottle and the maximum volume of blood that can be inoculated into each bottle, in consideration of the critical diagnostic variables of both blood volume (1, 7, 11, 20, 25, 32–34) and blood dilution (2, 27, 34). For most adult patients, it has been recommended that each culture set be inoculated with at least 10 ml of blood (5 ml per bottle [1]) and preferably with 20 to 30 ml of blood (11, 33, 34) to maximize recovery of pathogens. A blood-to-broth dilution ratio ranging from 1:7 to 1:30 has provided acceptable recovery (27), and a dilution of at least 1:5 but preferably up to 1:10 has been recommended to reduce antibacterial activity in the blood to subinhibitory levels (2, 34).

The ESP system (Difco Laboratories, Detroit, Mich.) utilizes bottles containing a larger volume (80 ml) of broth than in other automated blood culture systems, allowing for the sampling of 10 ml of blood per bottle and a dilution ratio of 1:8 (12.5%, vol/vol). The aerobic medium is a modified tryptic soy broth, and the anaerobic medium is a supplemented proteose peptone broth containing hemin, cysteine, and vitamin K_1 (31). After an ESP bottle is inoculated, a connector is attached, which eliminates any vacuum or pressure and connects the bottle to a sensing probe when the bottle is placed into the ESP incubator module (31). The system detects microbial growth by monitoring (every 12 to 24 min) pressure changes in the headspace of each bottle, changes resulting from either production or consumption of gases, including CO_2, H_2, and N_2 (21, 30, 31). Aerobic cultures are continuously agitated at 160 rpm, while anaerobic bottles are incubated in a stationary mode. When significant changes in bottle headspace pressure, indicating microbial growth, are detected, a red light comes on both at the bottle's location within the incubator and on top of the incubator module.

A combination of the Isolator (Wampole Laboratories, Cranbury, N.J.) and an anaerobic broth bottle, each inoculated with up to 10 ml of blood, has been found by this and other laboratories to reliably detect pathogens in the blood, even following recent antibiotic therapy (9, 10, 13, 15, 39). However, both Isolator technology and routine bottle subculturing using needles and syringes are labor intensive, and the latter procedure is not without risk of injury to the laboratory's technologists. In an attempt to find an efficient, safe alternative to the Isolator-manual bottle blood culture system in use at York Hospital for the last 11 years, the ability of this system to detect all types (including mixtures) of microbial pathogens in the blood was compared with that of the two-bottle automated ESP system. Because of the expense of the ESP system (as well as that of the Isolator), the clinical impact of reports of blood culture results on changes in patients' therapy was also determined.

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MATERIALS AND METHODS

Collection of blood. During the study, the venipuncture site of each patient for whom blood cultures were ordered was

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decontaminated by a four-step process including application of tincture of green soap, 70% isopropyl alcohol, 10% providone-iodine, and 70% isopropyl alcohol. By using a syringe or a blood collection set (Becton Dickinson, Franklin Lakes, N.J.), approximately 40 ml of blood was collected by the laboratory's phlebotomists from each patient weighing more than 80 lb (ca. 36 kg) (each patient's total blood volume was >2,200 ml [12]). The blood was equally distributed among an Isolator, Thiol, and ESP aerobic and anaerobic bottles. Whenever possible, two complete blood culture sets were inoculated for each patient; this usually required considerably less than 3.6% of a patient's total blood volume (12), and the sets were usually collected one-half hour apart. If additional blood cultures (up to a total of four) were ordered on the same day by the physician, only an Isolator and a Thiol bottle were inoculated for each patient to conserve blood, and these cultures were not included in the study. Isolators and aerobic ESP bottles were inoculated first. The order of inoculation of both aerobic and both anaerobic devices was reversed weekly. Only blood culture sets with at least 7 ml of blood in each device were included in the study.

Processing of cultures. Isolators were processed and all bottles were incubated within 30 min of blood collection. Isolators were centrifuged at 3,000 × *g* for 30 min and processed according to the manufacturer's instructions. The sediment (about 1.5 ml) was inoculated equally onto two 5% sheep blood agar plates and two chocolate agar plates. All Isolator cultures were incubated aerobically (5 to 10% CO_2) at 35°C; one sheep blood and one chocolate agar culture were incubated for 4 days, and the remaining cultures were incubated for 6 days, with once-daily examination. All bottles were incubated for 8 days at 35°C. Thiol bottles were examined once daily for evidence of microbial growth and were routinely subcultured to anaerobically incubated chocolate agar plates after both 2 and 8 days of incubation. ESP aerobic and anaerobic bottles were routinely subcultured on the 8th day to aerobically and anaerobically incubated chocolate agar plates, respectively. All subculture plates were incubated for 48 h with daily inspection. ESP bottles flagged as positive by the system were Gram stained and subcultured between 8 and 9 a.m., 11 a.m. and 12 p.m., and 3 and 4 p.m. daily. Positive Isolator cultures and macroscopically positive Thiol bottles were Gram stained and subcultured once daily. Microbial isolates were identified by routine biochemical, serological, and (for anaerobes) chromatographic methods (3).

Determination of clinical significance. The clinical significance of isolates was determined by physicians (J.P.M., K.S.P., and S.L.S.) participating in the study. Previously published guidelines used to determine significance included the species identification, number of positive devices or culture sets, relative detection time, recovery of the same species from a different site, clinical signs and symptoms, major comorbidity, predisposing factors, and a favorable response to antibiotics (1, 4, 5, 8, 17, 32, 37, 38). *Corynebacterium* species, *Propionibacterium* species, *Bacillus* species, and coagulase-negative staphylococci recovered from only one culture device were considered to be contaminants (1, 4, 29).

The *Z* test for differences in proportions for independent samples was used for statistical analysis of results (35). A *P* value of <0.05 was selected as the minimum level of significance.

RESULTS

From 7 December 1992 until 3 December 1993, 7,070 adequately filled blood culture sets were collected from 2,841 patients (age range, 6 to 101 years; mean, 60.7 years; median, 66 years). A total of 1,054 isolates were recovered, but only 607 (57.6%) were considered to be associated with infection. These 607 isolates were recovered from 529 (7.5%) of the cultures collected and from 286 (10.1%) of the patients studied. Patients with clinically significant isolates ranged in age from 18 to 97 years (mean, 66.3 years; median, 70 years). The mortality rate for patients with significant isolates was 9.4%. Contaminants were recovered from 335 (4.7%) of the Isolators compared with only 20 (0.3%) of the Thiol bottles, 59 (0.8%) of the ESP aerobic bottles, and 33 (0.5%) of the ESP anaerobic bottles. The contamination rate for the Isolator was significantly greater than that for any bottle ($P < 0.001$). From 7 December 1992 until 26 March 1993, false-positive signals were associated with 36 (1.7%) of 2,126 aerobic ESP bottles and with 317 (14.9%) of 2,126 anaerobic ESP bottles. This unacceptably high rate of false-positive signals was reduced following changes made by the manufacturer in the ESP software and/or hardware on 26 March 1993 and again on 26 June 1993. From 27 March 1993 until the end of the study, false-positive ESP signals were associated with 89 (1.8%) of 4,944 aerobic bottles and 77 (1.6%) of 4,944 anaerobic bottles.

Significantly more total isolates of pathogens were recovered with the Isolator than with any of the three types of bottles ($P < 0.001$ for each bottle) (Table 1). Significantly more isolates of members of the family *Enterobacteriaceae* ($P < 0.001$), *Pseudomonas aeruginosa* ($P < 0.05$), *Staphylococcus aureus* ($P < 0.05$), and *Staphylococcus* spp. (coagulase negative) ($P < 0.001$) were recovered with the Isolator than with any bottle. The ESP anaerobic bottle, however, accounted for the detection of significantly more isolates of *Streptococcus pneumoniae* than did the Isolator ($P < 0.05$). Predictably, more *Candida* spp. were recovered with the Isolator than with either Thiol ($P < 0.001$) or the ESP anaerobic bottle ($P < 0.05$), and more anaerobes were recovered with the two anaerobic bottles than with the Isolator ($P < 0.001$ for each bottle). The differences in recovery of total pathogens among the three types of bottles (Thiol, ESP aerobic, and ESP anaerobic) were not significant. Significantly more total isolates of pathogens ($P < 0.001$) as well as members of the family *Enterobacteriaceae* ($P < 0.001$), *S. aureus* ($P < 0.01$), *Staphylococcus* spp. (coagulase negative) ($P < 0.01$), and *Enterococcus* spp. ($P < 0.05$) were detected with the conventional system (Isolator plus Thiol), while the ESP two-bottle system yielded significantly more isolates of *S. pneumoniae* ($P < 0.01$) (Table 2). The conventional blood culture system allowed for detection of significantly more total episodes of bacteremia or fungemia ($P < 0.001$) (Table 3), as well as episodes due to members of the family *Enterobacteriaceae* ($P < 0.001$), *Enterococcus* spp. ($P < 0.01$), and yeasts ($P < 0.05$). The difference between the conventional and ESP systems in detection of bacteremic episodes due to *S. pneumoniae* was not significant.

Of 456 significant isolates which were recovered with the Isolator, 230 (50.4%) resulted in counts of ≤1.0 CFU/ml of blood, and 83 (18.2%) yielded only one colony (0.1 CFU/ml) (Table 4). There was a direct relationship between the colony counts of isolates recovered with the Isolator and the ability to detect these same isolates in each type of bottle. For example, only 21 (25.3%) of 83 isolates recovered with the Isolator at 0.1 CFU/ml of blood, compared with 94 (90.4%) of 104 isolates recovered with the Isolator at 1.1 to 10 CFU/ml of blood, were detected in the ESP aerobic bottles.

In our patient population, polymicrobic bacteremia was detected in specimens from 34 (11.9%) of the patients from whom pathogens had been recovered and in 58 (11.0%) of the positive cultures. The mortality rate for those patients with

TABLE 1. Pathogens recovered with Isolator, Thiol, and ESP aerobic and anaerobic bottles

Organism(s) (*n*)	No. (%) of isolates recovered with:			
	Isolator[a]	Thiol broth bottle	ESP aerobic bottle	ESP anaerobic bottle
Enterobacteriaceae				
Escherichia coli (140)	114 (81.4)	80 (57.1)[b]	95 (67.9)[c]	62 (44.3)[b]
Klebsiella pneumoniae (38)	28 (73.7)	23 (60.5)	17 (44.7)[c]	15 (39.5)[c]
Other (56)	48 (85.7)	38 (67.9)[d]	40 (71.4)	31 (55.4)[b]
Total (234)	190 (81.2)	141 (60.3)[b]	152 (65.0)[b]	108 (46.2)[b]
P. aeruginosa (16)	13 (81.3)	0[b]	8 (50.0)[d]	1 (6.3)[b]
Other gram-negative species (11)	9 (81.8)	4 (36.4)[d]	9 (81.8)	4 (36.4)[d]
Staphylococcus spp.				
S. aureus (70)	57 (81.4)	41 (58.6)[c]	44 (62.9)[d]	43 (61.4)[c]
Coagulase negative (67)	63 (94.0)	36 (53.7)[b]	46 (68.6)[b]	40 (59.7)[b]
Total (137)	120 (87.6)	77 (56.2)[b]	90 (65.7)[b]	83 (60.6)[b]
Streptococcus spp.				
S. pneumoniae (32)	22 (68.8)	18 (56.3)	22 (68.8)	29 (90.6)[d]
Viridans group (25)	24 (96.0)	23 (92.0)	20 (80.0)	24 (96.0)
Other (40)	31 (77.5)	26 (65.0)	33 (82.5)	27 (67.5)
Total (97)	77 (79.4)	67 (69.1)	75 (77.3)	80 (82.5)
Enterococcus spp. (33)	25 (75.8)	19 (57.6)	20 (60.6)	19 (57.6)
Other gram-positive species (7)	7 (100)	2 (28.6)[d]	5 (71.4)	4 (57.1)[d]
Anaerobes				
Bacteroides spp. (26)	0	19 (73.1)	5 (19.2)	22 (84.6)
Clostridium spp. (8)	1 (12.5)	6 (75.0)	1 (12.5)	7 (87.5)
Other (23)	1 (4.3)	18 (78.3)	3 (13.0)	14 (60.9)
Total (57)	2 (3.5)	43 (75.4)[b]	9 (15.8)	43 (75.4)[b]
Candida spp. (15)	13 (86.7)	0[b]	9 (60.0)	4 (26.7)[d]
Total (607)	456 (75.1)	353 (58.2)[b]	377 (62.1)[b]	346 (57.0)[b]

[a] Isolator-inoculated culture plates were incubated only aerobically (5 to 10% CO_2).
[b] The difference compared with the Isolator is significant at the $P < 0.001$ level.
[c] The difference compared with the Isolator is significant at the $P < 0.01$ level.
[d] The difference compared with the Isolator is significant at the $P < 0.05$ level.

polymicrobic bacteremia was 23.5% (8 of 34), while the rate for patients with monomicrobial sepsis was only 7.5% (19 of 252) ($P < 0.05$). Of 134 isolates from polymicrobic cultures, 87 (64.9%) were detected with the Isolator, 80 (59.7%) were detected with the Thiol, and 64 (47.8%) and 76 (56.7%) were detected with ESP aerobic and anaerobic bottles, respectively. Anaerobes accounted for 32 (23.9%) of the isolates from polymicrobic cultures. These 32 isolates of anaerobes represented over half (56.1%) of the 57 anaerobes recovered during the study. Overall, anaerobes were recovered from 28 (9.8%) of the patients with pathogens and from 43 (8.1%) of the positive cultures. The mortality rate for those patients whose blood contained anaerobes was 21.4% (6 of 28), while the rate for patients with sepsis due only to aerobic or facultatively anaerobic pathogens was only 8.1% (21 of 258) (not significant). Yeasts were detected in specimens from 9 (3.1%) of the positive patients and in 15 (2.8%) of the positive cultures.

When all four devices were positive for the same pathogen, the mean detection times were 21.8, 46.6, 24.6, and 41.2 h for Isolator, Thiol, and ESP aerobic and anaerobic bottles, respectively. ESP times are those when positive bottles were removed for workup, which averaged approximately 5 h after the bottles

TABLE 2. Pathogens recovered with the conventional system (Isolator and Thiol) and with the ESP system (aerobic and anaerobic bottles)

Organism(s) (*n*)	No. (%) of significant isolates recovered by using:			*P*[a]
	Conventional system alone	ESP system alone	Both systems	
Enterobacteriaceae (234)	72 (30.8)	20 (8.5)	142 (60.7)	<0.001
P. aeruginosa (16)	7 (43.8)	3 (18.8)	6 (37.5)	NS
Other gram-negative species (11)	1 (9.1)	1 (9.1)	9 (81.8)	NS
S. aureus (70)	19 (27.1)	6 (8.6)	45 (64.3)	<0.01
Staphylococcus spp., coagulase-negative (67)	14 (20.9)	3 (4.5)	50 (74.6)	<0.01
S. pneumoniae (32)	1 (3.1)	8 (25.0)	23 (71.9)	<0.01
Viridans streptococci (25)	1 (4.0)	0	24 (96.0)	NS
Other streptococci (40)	4 (10.0)	6 (15.0)	30 (75.0)	NS
Enterococcus spp. (33)	12 (36.4)	4 (12.1)	17 (51.5)	<0.05
Other gram-positive species (7)	2 (28.6)	0	5 (71.4)	NS
Anaerobes (57)	12 (21.1)	12 (21.1)	33 (57.9)	NS
Yeasts (15)	4 (26.7)	2 (13.3)	9 (60.0)	NS
Total (607)	149 (24.5)	65 (10.7)	393 (64.7)	<0.001

[a] The proportion of a species or group detected with the conventional system was compared with the proportion detected with the ESP system. NS, not significant.

TABLE 3. Episodes of bacteremia or fungemia detected with the conventional system (Isolator and Thiol) and with the ESP system (aerobic and anaerobic bottles)

Organism(s) (*n*)	No. (%) of patients with isolates recovered with:			*P*[a]
	Conventional system alone	ESP system alone	Both systems	
Enterobacteriaceae (131)	35 (26.7)	11 (8.4)	85 (64.9)	<0.001
P. aeruginosa (9)	4 (44.4)	1 (11.1)	4 (44.4)	NS
Other gram-negative species (6)	1 (16.7)	1 (16.7)	4 (66.7)	NS
S. aureus (34)	7 (20.6)	4 (11.8)	23 (67.6)	NS
Staphylococcus spp., coagulase-negative (31)	5 (16.1)	2 (6.5)	24 (77.4)	NS
S. pneumoniae (19)	1 (5.3)	5 (26.3)	13 (68.4)	NS
Viridans streptococci (9)	0	0	9 (100)	NS
Other streptococci (24)	3 (12.5)	3 (12.5)	18 (75.0)	NS
Enterococcus spp. (22)	10 (45.5)	2 (9.1)	10 (45.5)	<0.01
Other gram-positive species (3)	1 (33.3)	0	2 (66.7)	NS
Anaerobes (38)	10 (26.3)	8 (21.1)	20 (52.6)	NS
Yeasts (9)	4 (44.4)	0	5 (55.6)	<0.05
Total (335)	81 (24.2)	37 (11.0)	217 (64.8)	<0.001

[a] The proportion of bacteremic or fungemic episodes due to a species or group which was detected with the conventional system was compared with the proportion detected with the ESP system. NS, not significant.

were first detected as positive by the ESP system. When a time to detection of ≥24 h earlier in one system was counted as an earlier detection time, there were no significant differences in detection of any microbial species or group between the two blood culture systems. Of 286 patients with clinical and microbiological evidence of infection, pathogens from only 4 (1.4%) were detected only following terminal subculture of the bottles. In all, 28 (7.9%) of 353 isolates from Thiol, 2 (0.5%) of 377 isolates from the ESP aerobic bottle, and 19 (5.5%) of 346 isolates from the ESP anaerobic bottle were detected only after terminal subculture. Most of these isolates, however, had already been recovered from other devices in culture sets from the same patients.

Antimicrobial agents had been administered within 4 days of obtaining the blood cultures to 72 (25.2%) of the 286 patients with culture-proven bacteremia or fungemia, including 5 (17.8%) of 28 patients from whose blood anaerobes were recovered and 7 (20.6%) of 34 patients with polymicrobic bacteremia. Following reports of positive blood cultures, therapy was initiated or changed for 160 (55.9%) of the patients, including 10 (35.7%) of the patients with anaerobic bacteremia and 19 (55.9%) of those with polymicrobic bacteremia.

DISCUSSION

In the current study, the Isolator resulted in the detection of 21 and 32% more pathogens than the ESP aerobic and ESP anaerobic bottles, respectively. However, no single blood culture device detected more than 75% of the significant microbial isolates, a finding very similar to that of a previous study with the Isolator (10). The finding of improved detection of many species of pathogens (except for *S. pneumoniae*) related to use of the Isolator, compared with conventional broth media, is similar to previous reports from this and other laboratories (10, 13, 15, 39). Enhanced detection of pathogens with the Isolator is the result of the ability of Isolator technology to allow removal of microorganisms from antibiotics and other antimicrobial substances in the blood (9, 34, 39). Since approximately one-quarter of our culture-positive patients had been pretreated with antibiotics before blood cultures were collected (compared with pretreatment in 56% of the sepsis syndrome episodes in another study [14]), this advantage of the Isolator was particularly useful for our patient population. The main clinical advantage of our conventional blood culture system (Isolator and Thiol) was the superior detection of many types of pathogens. Advantages of the ESP two-bottle system included a significantly lower contamination rate (compared with the Isolator), the detection of more isolates of *S. pneumoniae*, and the elimination of the need for labor-intensive (and potentially dangerous) routine terminal subcultures of bottles, a process requiring the use of syringes and needles. Even though ESP bottles which were flagged as positive by the system were removed and worked up three times each day, compared with a once-per-day workup of positive Isolator or Thiol cultures, the ESP system did not provide a significant reduction (≥24 h) in detection time for any microbial pathogen. The Isolator contamination rate found in the current study (4.8%) is well within the range of contamination rates for the device, as previously reviewed (39).

TABLE 4. Relationship of quantitative recovery with Isolator to detection of pathogens in bottles

Isolator colony count (CFU/ml)	No. (%) of Isolator-recovered pathogens	No. (%) of pathogens recovered with Isolator and also recovered with:		
		Thiol bottle	ESP aerobic bottle	ESP anaerobic bottle
0.1	83 (18.2)	17 (20.5)	21 (25.3)	17 (20.5)
0.2	39 (8.6)	14 (35.9)	18 (46.2)	12 (30.8)
0.3–0.5	61 (13.4)	31 (50.8)	36 (59.0)	27 (44.3)
0.6–1.0	47 (10.3)	28 (59.6)	39 (83.0)	27 (57.4)
1.1–10	104 (22.8)	70 (67.3)	94 (90.4)	83 (79.8)
>10	122 (26.8)	107 (87.7)	115 (94.3)	107 (87.7)

Of the pathogens detected by the Isolator, 50% were recovered in counts of ≤1.0 CFU/ml of blood, and 18% were recovered only as a single colony (Table 4). These findings are almost identical to our previous experience with the Isolator (13) and are also similar to other previous reports (10, 15). False-negative ESP and Thiol broth cultures were predictably most frequently accompanied by counts of ≤1.0 CFU/ml of blood on positive Isolator cultures, an observation noted previously when other bottle systems were used (13, 15). The critical consideration of blood volume required for the detection of low concentrations of pathogens was further underscored by the fact that pathogens from 63 (26%) of our

culture-positive patients from whom two complete culture sets were collected were recovered from only one of the eight devices used in the two sets (11b). This finding of a significant percentage of septic patients for whom only one blood culture device was positive is similar to reports from other clinical studies (18, 26). In our patient population (primarily elderly, with many pretreated with antimicrobial agents), therefore, it appears that a large blood volume (20 to 30 ml) as well as two or three culture devices per culture set and two or three culture sets per patient are required to provide satisfactory detection of pathogens from patients with low-level sepsis. The blood volume apparently required for our patient population is similar to that recommended in some previous reports (11, 33, 34) but larger than that found to be necessary in another (37). In the latter study, 99% of the episodes of sepsis were detected when a total of 30 ml of blood was cultured.

In the current study, multiple pathogens were recovered from 12% of the patients with bacteremia or fungemia. Polymicrobic bacteremia has been reported to occur in 7 to 18% of patients with sepsis (8, 10, 14, 24, 36, 37) and was more likely to be hospital acquired, to come from bowel or multiple foci, and to be found in patients with nonhematologic malignancies or multiple underlying diseases (36). The incidence of polymicrobic bacteremia has been increasing steadily in this country because of factors including increased numbers of immunosuppressed patients, aggressive surgical techniques, and the use of intravascular medical devices (39). Both the volume of blood and types of culture devices employed to detect all organisms responsible for polymicrobic bacteremia are clinically important considerations because a knowledge of the occurrence and type of such an infection helps with the selection of the most appropriate therapy and can suggest a source of the organisms or an underlying disease (5, 36, 39). In previous studies, patients with polymicrobic bacteremia were found to have a significantly increased risk of dying from sepsis compared with those with monomicrobial bacteremia (24, 36), findings similar to the results of the current study. The failure to use appropriate antibiotics for all microorganisms recovered from a patient has been reported to be associated with an increased mortality rate (36). In the current study, therapy was initiated or changed for over half (56%) of our patients with polymicrobic sepsis following the laboratory's report of multiple isolates recovered from the blood.

In contrast to recent reports of a declining and relatively infrequent recovery of anaerobes (6, 8, 16, 23, 28, 29), these pathogens were recovered from 28 (9.8%) of our patients with bacteremia or fungemia, a result similar to our findings reported in 1984 (13). Although some studies have found that laboratory reports of positive blood cultures containing anaerobes infrequently influenced the clinical management of the patients (16, 23), antimicrobial therapy for over one-third (35.7%) of our patients with anaerobic bacteremia was changed following the laboratory's reports. Culturing a sufficient volume of blood is as critical for detection of anaerobes as it is for that of other pathogens (7). This point was underscored for our patients by the finding that only 75% of the isolates of anaerobes were recovered with either Thiol or the ESP anaerobic bottle, each inoculated with 10 ml of blood. Anaerobic species are more likely to be detected in cases of polymicrobic infections (36), as was the case during the current study. It has been suggested by some (22, 23, 28, 29), but not others (19), that two aerobic bottles should be used for routine blood cultures and that anaerobes should be sought only selectively, at the request of the attending physicians. From the results of the current study, including the detection of anaerobes from the blood of 1 in 10 patients with sepsis and the finding that therapy was changed for over one-third of the patients following laboratory reports of the presence of anaerobes, we believe that the ability to routinely detect anaerobes continues to be clinically important for our community hospital's patient population. Recovery of anaerobes may vary from one patient population to another (29).

A problem with a relatively high rate of ESP false-positive signals has been previously reported (21). It appears that this problem has been controlled, if not completely corrected, by the manufacturer during the last 8 months of the current study. In addition, ESP contamination rates of 0.8 and 0.5% for the aerobic and anaerobic bottles, respectively, as found in the current study, were approximately half those described previously (21) and appear to be acceptably low.

In summary, no single blood culture system currently available provides for 100% detection of pathogens (10, 13, 15). The ESP system was associated with a contamination rate significantly lower than that with the Isolator and provided an automated culture technology for which routine and terminal subcultures were not required. In addition, the large volume of ESP broth (80 ml) accommodated a large volume (10 ml) of blood at a dilution of 1:8 (12.5%, vol/vol), considerations which may be important for the detection of low-level bacteremia (1, 2, 7, 11, 20, 25, 27, 32, 34). However, continued use of the Isolator with our patient population to remove antimicrobial substances from the blood seems clinically prudent. Further studies of the ESP and other automated systems (compared with conventional bottles as well as with devices which remove or inactivate antimicrobial agents) in different patient populations and in different geographical regions are to be encouraged. These studies should lead to a more thorough understanding of possible advantages or disadvantages of each system for detection of all pathogens, as well as anaerobes, and the variation that may be encountered in the latter on the basis of differences in population, blood volume cultured, and type of medium used.

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