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Clinical Importance of Increased Sensitivity of BacT/Alert FAN Aerobic and Anaerobic Blood Culture Bottles

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Two recent multicenter blood culture studies found that BacT/Alert FAN (FAN) bottles (Organon Teknika, Durham, N.C.) had increased yields in detecting bacteremia and fungemia compared with standard BacT/Alert (STD) bottles. Because the clinical importance of this increase in microbial recovery is unknown, we performed a retrospective analysis to determine the frequency with which FAN bottles were the sole means of detecting an episode of bacteremia. There were 1,047 positive blood cultures in which both study bottles were adequately filled and the organism isolated was judged to be the cause of sepsis: 240 (23%) were positive only in FAN bottles and 73 (7%) were positive only in STD bottles. Of a total of 664 episodes of bacteremia, 126 (19%) were identified only by FAN bottles and 43 (7%) were identified only by STD bottles ($P < 0.0001$). Episodes detected only by FAN bottles more often were recurrent events (23 of 126, or 18%) than episodes detected only by STD bottles (2 of 43, or 5%) ($P < 0.05$) and more commonly occurred in patients receiving theoretically effective antibiotic therapy (33 of 126 [26%] versus 4 of 43 [9%]) ($P < 0.05$). The medical records for patients with 127 of these episodes (92 FAN bottles only; 35 STD bottles only) were available for review. More than half of both FAN bottle-only (60 of 92, or 65%) and STD bottle-only (20 of 35, or 57%) episodes were judged to be clinically important. We conclude that FAN bottles improve the detection of bacteremia and that the majority of the additional episodes detected are clinically important. The benefits of the greater yield in specific patient populations must be balanced against the higher costs of FAN bottles.

Even before the era of commercially available automated blood culture systems, specialized formulations of culture media as well as specimen processing techniques had been developed with the hope of improving the detection of bacteremia and fungemia. The impetus for this development was the perceived need to increase the recovery of either specific pathogens (e.g., specialized media for fungi, mycobacteria, and other fastidious organisms) or microorganisms whose growth has been inhibited by antimicrobial agents present in the patient. Approaches to negating antimicrobial activity include the use of resin-containing media, pretreatment of blood for culture with a resin-based Antimicrobial Removal Device (Marion Laboratories, Kansas City, Mo.), and lysis-centrifugation to separate microorganisms from serum. Although some of these measures have proven effective either in enabling the growth of fungi and staphylococci (1, 5, 7, 13, 17, 27) or in removing antibiotics from the growth environment (10, 15, 19), their ability consistently to detect more cases of bacteremia and fungemia has been less certain or even refuted (12, 20, 31). A still more important question remains whether the observed increase in detection rates is clinically important and, if so, under what clinical circumstances (6, 10, 11, 14).

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The BacT/Alert blood culture system, introduced several years ago with aerobic and anaerobic formulations of a tryptic soy broth base (22), performed well in an initial controlled clinical trial (29). Recently, the manufacturer introduced new aerobic and anaerobic media (FAN media) composed of brain heart infusion broth and Ecosorb, a proprietary substance that, among other components, contains absorbent charcoal and Fuller's earth. These media were developed to enhance the recovery of fastidious organisms from blood as well as to improve the detection of bacteremia and fungemia, especially in patients receiving antimicrobial agents. Two recent clinical trials have demonstrated the improved yield of bacteria (24, 30), and fungi (24) by using FAN bottles compared with standard (STD) BacT/Alert blood culture bottles. We report here further analyses of the data from those two studies, including a review of patient clinical records to determine how many additional episodes of bacteremia and fungemia were detected only by FAN bottles and whether such detection was clinically important.

MATERIALS AND METHODS

Collection and processing of samples. The collection and processing of samples have been described previously (24, 30) and will only be summarized here. Blood obtained from a single venipuncture (30 ml total) was distributed equally in 10-ml aliquots to each of three BacT/Alert bottles in a set. In the FAN aerobic study these were an STD aerobic bottle, a FAN aerobic bottle, and an STD anaerobic bottle. In the FAN anaerobic study the three bottles were an STD aerobic bottle, an STD anaerobic bottle, and a FAN anaerobic bottle. The

TABLE 1. Microorganisms and septic episodes detected by only FAN or STD bottles

Microorganism	No. of episodes						*P* value
	Aerobic study		Anaerobic study		Combined studies		
	FAN bottle	STD bottle	FAN bottle	STD bottle	FAN bottle	STD bottle	
Staphylococcus aureus	13	1	29	3	42	4	<0.0001
Coagulase-negative staphylococci	11	1	9	1	20	2	<0.0005
Members of the family *Enterobacteriaceae*	8	3	14	2	22	5	<0.005
Nonfermenting gram-negative rods	2	5	0	1	2	6	NS[a]
All other bacteria	7	3	5	3	12	6	NS
Anaerobes	2	1	3	4	5	5	NS
Fungi	7	4	0	3	7	7	NS
Polymicrobial[b]	7	3	9	5	16	8	NS
Total episodes	57	21	69	22	126	43	<0.0001
Recurrent episodes	9	0	14	2	23	2	<0.05
Episodes among patients on therapy[c]	10	3	23	1	33	4	<0.05

[a] NS, not significant.
[b] At least one organism of a polymicrobial episode detected only in a single bottle type.
[c] Microorganism(s) detected from a patient known to be on therapy theoretically effective for that microorganism(s).

volume of each bottle was measured to ensure that they were inoculated with the specified adequate (8- to 12-ml) volume. Unless macroscopic growth was evident upon receipt of the bottles in the laboratory, all bottles were placed in the BacT/Alert instrument and were processed according to the manufacturer's instructions. When growth was detected, all microorganisms were identified by standard microbiologic procedures (2).

Analysis of data. A record for each blood culture set in which at least one bottle was positive was entered in a computer database (Paradox; Borland International, Scotts Valley, Calif.). Recorded data included which bottles of the set were received, the volume of blood inoculated into each bottle, the date of receipt in the laboratory, the identity of the microorganism(s) recovered, and the time to detection (in hours) of each positive bottle. Determinations as to whether each isolate represented a contaminant versus a true cause of bacteremia, as well as whether the patient was on therapy inhibitory to the microorganism, were made by an infectious disease physician. A patient was considered to have an episode of bacteremia or fungemia when successive positive blood samples drawn from a single patient were positive within 48 h of each other, as defined by Weinstein et al. (26) and modified by Towns et al. (23). In order for a specific bottle (FAN or STD bottle) to be considered the only one detecting either a contaminant or an episode of bacteremia or fungemia, the positive bottle had to be part of a set in which both study bottles were adequately filled and the third bottle (i.e., nonstudy standard BacT/Alert bottle) was negative for the organism. All comparisons were evaluated statistically by either McNemar's test for paired observations (16), the χ^2 test, or Fisher's exact test when small values were compared.

Clinical record review. The available medical records of patients whose episodes of bacteremia or fungemia were detected by only STD or FAN bottles were reviewed to determine the clinical importance of each episode. To be judged clinically important, an isolate had to represent true bacteremia or fungemia requiring treatment. When, on culture, samples other than blood defined the presence and etiology of the bloodstream infection, the episode was considered not important if appropriate therapy could have been determined from cultures of those samples. In addition, clinically important episodes had to meet one of the following criteria: either the patient was on inappropriate (or no) antibiotic therapy when the blood sample for culture was drawn and survived until therapy could be initiated or the patient was on appropriate antibiotic therapy when the blood sample for culture was drawn and the positive result was used to modify the duration of therapy or trigger additional diagnostic or therapeutic measures. Since our results showed an increased number of contaminants recovered only from FAN bottles, we also evaluated whether this increased detection of contaminants may have had an adverse clinical impact. To do this we reviewed a subset (based upon the medical record number and availability) of medical records at one of the participating institutions (Duke University Medical Center) from patients whose specimens were positive for contaminating coagulase-negative staphylococci in only one study bottle (FAN or STD bottle).

RESULTS

A total of 14,541 adequately filled blood culture sets were processed during the clinical trials with aerobic and anaerobic FAN bottles. There were 1,047 positive cultures in which the microorganisms isolated represented sepsis, of which 240 (23%) were positive only in FAN bottles and 73 (7%) were positive only in STD bottles. Of a total of 664 episodes of bacteremia and fungemia, 169 were detected in one or the other bottle only: 126 (19%) were detected by FAN bottles and 43 (7%) were detected by STD bottles ($P < 0.0001$). The microorganisms responsible for septic episodes in each study, as well as in the combined studies, are listed in Table 1. A total of 750 contaminants (Table 2) were detected in the two studies; 222 (30%) were recovered from FAN bottles only and 121 (16%) were recovered from STD bottles only ($P < 0.0001$).

Medical records were reviewed for 127 (75%) of all patient episodes detected by only a single bottle type in the two studies, including 92 of 126 (73%) episodes detected only by FAN bottles and 35 of 43 (81%) detected only by STD bottles. Sixty (65%) of the FAN bottle-only episodes and 20 (57%) of the STD bottle-only episodes were judged to be clinically important (Table 3). The 60 clinically important episodes detected only by FAN bottles were more likely to be recurrent episodes (the same microorganism that was recovered during a prior episode in the same patient) and to occur in patients receiving antimicrobial therapy. In contrast, most clinically important episodes detected only by STD bottles were in patients not receiving antimicrobial therapy. Clinically important episodes

TABLE 2. Contaminants recovered from FAN or STD bottles

Microorganisms	No. of episodes						*P* value
	Aerobic study		Anaerobic study		Combined studies		
	FAN bottle	STD bottle	FAN bottle	STD bottle	FAN bottle	STD bottle	
Coagulase-negative staphylococci	101	42	59	37	160	79	<0.0001
Other contaminants[a]	35	20	27	22	62	42	NS[b]
Total	136	62	86	59	222	121	<0.0001

[a] *Propionibacterium* sp., *Corynebacterium* sp., and *Bacillus* sp. accounted for the majority of other contaminants.
[b] NS, not significant.

TABLE 3. Characteristics of clinically important episodes detected by only FAN or STD bottles

Characteristic	No. (%) of episodes		*P* value
	FAN bottle only	STD bottle only	
Microorganisms			
Staphylococcus aureus	20 (33)	2 (10)	<0.05
Coagulase-negative staphylococci	9 (15)	1 (5)	NS[a]
Members of the family *Enterobacteriaceae*	13 (22)	4 (20)	NS
Other microorganisms	7 (12)	7 (35)	<0.05
Polymicrobial[b]	11 (18)	6 (30)	NS
Total episodes	60 (100)	20 (100)	
Clinical variables			
Nosocomial	35 (58)	12 (60)	NS
Recurrent	15 (25)	0	<0.005
Antimicrobial therapy			
None	24 (40)	13 (72)	<0.05
Not adequate	16 (27)	2 (11)	NS
Adequate	20 (33)	3 (17)	NS
Unknown	0	2	

[a] NS, not significant.
[b] At least one microorganism of a polymicrobial episode detected in a single bottle type.

detected only by either FAN or STD bottles also were compared regarding patient age, sex, number of cultures drawn, specialty service, predisposing factors, source of bacteremia, temperature, leukocyte count, presence of hypotension, and outcome. No significant differences were found between FAN bottle-only and STD bottle-only episodes for any of these factors (data not shown). The reasons why the episodes were judged to be not clinically important, as well as the microorganisms isolated, are summarized in Table 4. Episodes detected only by FAN bottles more often were judged not to be clinically important because the patients already were receiving appropriate therapy and no other changes in therapy were made on the basis of the positive FAN bottle cultures.

Of the 31 episodes of coagulase-negative staphylococcal contamination reviewed, 7 of 21 (33%) that occurred only in FAN bottles and 4 of 10 (40%) that occurred only in STD bottles contributed either to unnecessary diagnostic studies or to superfluous antibiotic therapy.

DISCUSSION

Our review of bacteremic episodes provides evidence that use of FAN bottles versus STD bottles has a measurable impact on patient care. Since FAN bottles were designed to accomplish some of the same objectives as resin-containing media, we looked to the literature for previous reports regarding the clinical importance of increased yields with resin-containing media (6, 10, 11, 14). Jessamine et al. (11) reviewed 82 isolates recovered by BACTEC NR16A and NR17A resin bottles from 38 patients and concluded that there was no clinical impact resulting from the use of resin bottles. This, however, was not a controlled comparison of resin-containing versus routine media. For 22 of the patients receiving antibiotics to which the isolate was resistant, it was concluded that the resin media were superfluous on the basis of the assumption that isolates would have grown in non-resin-containing media if they had been inoculated into such media, yet this was demonstrated for only five patients whose specimens were inoculated into both routine and resin media (11). Our results do not support this observation, since more clinically important episodes in patients on inadequate antibiotic therapy were detected only by FAN bottles rather than by STD bottles (16 versus 2, respectively) (Table 3).

Another 18 patients in the study by Jessamine et al. (11) were receiving antimicrobial agents (to which the microorganism was susceptible) by the time that blood culture results were available. It was concluded that positive resin cultures did not contribute to patient care, since the patients were already on appropriate therapy that was not changed after the report of a positive blood culture. Moreover, for 10 of these patients the microorganism was recovered from a non-resin-containing culture of blood drawn prior to the beginning therapy. No mention was made, however, about the effect that isolation of an etiologic microorganism had among the patients without previous positive cultures (eight patients) either in determining the proper duration of therapy or in allowing the clinician to forgo further diagnostic testing. Hopfer et al. (10) reviewed the charts of 18 patients whose episodes of bacteremia were de-

TABLE 4. Characteristics of clinically unimportant episodes detected by only FAN or STD bottles

Characteristic	No. (%) of episodes		*P* value
	FAN bottles only	STD bottles only	
Microorganisms			
Staphylococcus aureus	11 (34)	2 (13)	NS[a]
Coagulase-negative staphylococci	8 (25)	0	<0.05
Members of the family *Enterobacteriaceae*	3 (9)	0	NS
Other microorganisms	6 (19)	7 (47)	NS
Polymicrobial[b]	4 (13)	6 (40)	NS
Total episodes	32 (100)	15 (100)	
Patient did not survive until a necessary change in therapy could be instituted	5 (16)	5 (33)	NS
Patient already on appropriate therapy, no change in type or duration of therapy	9 (28)	0	<0.05
Cultures of other specimens defined the presence of bacteremia and responsible microorganism	10 (31)	4 (27)	NS
Contaminant[c] or transient bacteremia requiring no therapy	8 (25)	6 (40)	NS

[a] NS, not significant.
[b] At least one organism of a polymicrobial episode detected in a single bottle type.
[c] Some isolates initially considered as true causes of sepsis were reclassified as contaminants.

tected only with a resin-containing medium (a concurrent routine bottle was negative) and reported that "antibiotic therapy was changed for only 4 of the 18 patients." Again, no consideration was given to the impact that isolating an etiologic microorganism had, apart from the choice of antimicrobial therapy.

In our study we applied uniform criteria in assessing the clinical importance of septicemic episodes and found that the proportion of episodes that were clinically important was similar between episodes detected only by FAN bottles and those detected only by STD bottles (65 and 57%, respectively). This similarity was in part due to a recognition of the clinical usefulness of detecting bacteremia beyond simply choosing an antibiotic to which the microorganism is susceptible. Yet, despite this broader definition of clinical importance, a greater percentage of FAN bottle-only versus STD bottle-only episodes were found for patients already on appropriate therapy at the time that the sample for culture was obtained and for whom the positive culture did not contribute to any clinical decisions (Table 4).

Rather than the polymer resin beads found in both BACTEC resin bottles and the Antimicrobial Removal Device, FAN bottles contain the proprietary substance Ecosorb. In contrast to the antibiotic-removing ability documented with resin-containing media (10, 19) and with the Antimicrobial Removal Device (15), the results of modified serum bactericidal studies suggest that improved microbial recovery in FAN bottles is not due to inactivation of antimicrobial agents (24, 30). It is possible that the Ecosorb in the FAN medium absorbs toxic metabolites and serum inhibitors or that the richer broth used in FAN medium (brain heart infusion rather than the tryptic soy broth found in STD medium) may support the growth of more isolates under adverse conditions. FAN bottles may therefore increase microbial recovery by promotion of growth rather than inactivation of inhibitory antibiotics.

Although we were unable to review all episodes of bacteremia and fungemia detected only by FAN or STD bottles, our data suggest that more clinically important episodes were detected by FAN bottles. This holds true both for patients who were and those who were not receiving antimicrobial therapy at the time that blood was drawn for culture. Of 169 episodes detected by only one bottle type, approximately 60% were clinically important, or 76 of 126 FAN bottle-only episodes and 26 of 43 STD bottle-only episodes. Since the proportion of patients not receiving antimicrobial therapy at the time that blood was drawn for culture was 40% for FAN bottle-only and 72% for STD bottle-only episodes (Table 3), it can be estimated that 30 of 76 (39%) FAN bottle-only and 18 of 26 (69%) STD bottle-only clinically important episodes were among patients not receiving appropriate antimicrobial therapy. Conversely, 46 of 76 (61%) FAN bottle-only and 8 of 26 (31%) STD bottle-only clinically important episodes were among patients receiving antimicrobial therapy.

Along with the increased yield of microorganisms causing sepsis, FAN bottles detected nearly twice as many contaminants as STD bottles (Table 2). It is possible that the enriched medium used in FAN bottles may enhance the growth of contaminant microorganisms so that they are detected within the 7-day incubation period. Increased contamination rates with resin-containing media have not been emphasized previously (5, 7, 10, 25, 27, 28). Since the present study did not compare the FAN bottle medium with resin-containing media directly, it is not possible to say whether the increased contamination rates observed with FAN bottles are greater than those found with resins or were simply highlighted by our clinical analyses. Along with more contaminants, more episodes of clinically unimportant bacteremia were detected. This increase in the level of "background noise" might be expected with the use of a more sensitive yet no more specific technology.

In an era of managed care and cost-containment, a balance must be struck between the associated costs and potential benefits of any new diagnostic or therapeutic modality. In favor of using FAN media is the increased detection of bacteremia, a condition associated with marked increases in the cost of patient care as well as significant morbidity and mortality (18). Such increased yield contributes, in some cases, to important decisions about the type and duration of therapy, which may lead to improved outcomes. Such results may enable physicians to forgo further diagnostic studies, as recently demonstrated with rapid susceptibility testing (8). Moreover, the FAN aerobic medium also is more effective than standard media for the detection of fungemia (24).

Conversely, routine use of FAN media may result in increased costs. The media are more expensive and the laboratory incurs the additional cost of working up more clinically unimportant isolates and contaminants. More important, and yet more difficult to quantify, are the nonlaboratory costs associated with an increased recovery of clinically unimportant isolates and contaminants. These may include unnecessary diagnostic studies, superfluous antimicrobial therapy, or other therapeutic interventions initiated in response to the detection of these isolates. Instances of such adverse clinical effects due to the detection of clinically unimportant isolates causing bacteremia were not found in our reviews of FAN bottle-only and STD bottle-only episodes. Regarding the increased costs of contaminated blood cultures, Bates et al. (3) evaluated these and found that a contaminated blood culture was associated with a median of more than 4 days of excess hospitalization and more than $4,000 in additional patient charges. We sought to determine what effect the detection of contaminants had on a small subset of 31 patients. Although the numbers are too small to make valid comparisons, unnecessary therapy and interventions were frequently initiated in apparent response to contaminated blood cultures (30 to 40% of episodes).

Considering the many laboratory and other cost factors as well as potential benefits associated with the use of FAN media, clinical scenarios in which the FAN media may have their greatest benefit should be selected. For example, patients who are already receiving antimicrobial agents but who continue to show evidence of suspected bacteremia or sepsis may benefit from the use of FAN media. FAN media may also be useful for patients not receiving antimicrobial agents but for whom routine blood cultures remain negative. If contamination rates could be reduced, such as with tincture of iodine preparation of the skin at the venipuncture site (21), discontinuation of drawing samples for culture through indwelling lines (4), and the use of well-trained venipuncture teams (9), a compelling case could be made for the routine use of the aerobic FAN bottle, especially in hospitals where yeasts are commonly recovered from blood cultures.

REFERENCES

1. **Appleman, M. D., R. S. Swinney, and P. N. R. Heseltine.** 1982. Evaluation of the antibiotic removal device. J. Clin. Microbiol. **15:**278–281.
2. **Balows, A., W. J. Hausler, Jr., K. L. Herrmann, H. D. Isenberg, and H. J. Shadomy (ed.).** 1991. Manual of clinical microbiology, 5th ed. American Society for Microbiology, Washington, D.C.
3. **Bates, D. W., L. Goldman, and T. H. Lee.** 1991. Contaminant blood cultures and resource utilization: the true consequences of false-positive results. JAMA **265:**365–369.
4. **Bryant, J. K., and C. L. Strand.** 1987. Reliability of blood cultures collected from intravascular catheter versus venipuncture. Am. J. Clin. Pathol. **88:**113–116.
5. **Courcol, R. J., A. V. Durocher, M. Roussel-Delvallez, A. Fruchart, and G. R. Martin.** 1988. Routine evaluation of BACTEC NR-16A and NR-17A media. J. Clin. Microbiol. **26:**1619–1622.

6. **Doern, G. V.** 1994. Manual blood culture systems and the antimicrobial removal device. Clin. Lab. Med. **14:**133–147.
7. **Doern, G. V., and N. M. Gantz.** 1983. Detection of bacteremia in patients receiving antimicrobial therapy: and evaluation of the antimicrobial removal device and 16B medium. J. Clin. Microbiol. **18:**43–48.
8. **Doern, G. V., R. Vautour, M. Gaudet, and B. Levy.** 1994. Clinical impact of rapid in vitro susceptibility testing and bacterial identification. J. Clin. Microbiol. **32:**1757–1762.
9. **Halliday, B. E., and R. B. Schifman.** 1994. Effect of phlebotomy team on the quality of blood culture collections, abstr. C-147, p. 516. *In* Abstracts of the 94th General Meeting of the American Society for Microbiology 1994. American Society for Microbiology, Washington, D.C.
10. **Hopfer, R. L., D. G. Moore, V. Fainstein, S. Watkins, and M. Wengler.** 1983. Routine use of BACTEC 16B bottles to remove antibacterial and antitumor agents from blood cultures of cancer patients. J. Clin. Microbiol. **18:**759–764.
11. **Jessamine, P. G., D. J. Hoban, and K. R. Forward.** 1990. Positive Bactec resin cultures do not influence antimicrobial selection. Diagn. Microbiol. Infect. Dis. **13:**281–284.
12. **Kelly, M. T., F. J. Roberts, D. Henry, I. Geere, and J. A. Smith.** 1990. Clinical comparison of Isolator and BACTEC 660 resin media for blood culture. J. Clin. Microbiol. **28:**1925–1927.
13. **Kirkley, B. A., K. A. Easley, and J. A. Washington.** 1994. Controlled clinical evaluation of Isolator and ESP aerobic blood culture systems for detection of bloodstream infections. J. Clin. Microbiol. **32:**1547–1549.
14. **Levine, P., A. M. Yinnon, M. Hersch, and B. Rudensky.** 1994. Impact of resin bottle blood cultures on treatment of critically ill patients, abstr. D-13, p. 151. *In* Program and abstracts of the 34th Interscience Conference on Antimicrobial Agents and Chemotherapy. American Society for Microbiology, Washington, D.C.
15. **Lindsey, N. J., and P. E. Rieley.** 1981. In vitro antibiotic removal and bacterial recovery from blood with an antibiotic removal device. J. Clin. Microbiol. **13:**503–507.
16. **McNemar, Q.** 1962. Psychological statistics, 3rd ed., p. 209–239. John Wiley & Sons, Inc., New York.
17. **Peterson, L. R., C. J. Shanholtzer, M. L. Mohn, and D. N. Gerding.** 1983. Improved recovery of microorganisms from patients receiving antibiotics with the antimicrobial removal device. Am. J. Clin. Pathol. **80:**692–696.
18. **Pittet, D., D. Tarara, and R. P. Wenzel.** 1994. Nosocomial bloodstream infection in critically ill patients: excess length of stay, extra costs, and attributable mortality. JAMA **271:**1598–1601.
19. **Smith, S. M., and R. H. K. Eng.** 1985. Effectiveness of antibiotic removal by the antibiotic-binding blood culture systems. J. Clin. Microbiol. **3:**201–212.
20. **Strand, C. L.** 1982. Evaluation of the antimicrobial removal device when used with the BACTEC blood culture system. Am. J. Clin. Pathol. **78:**853–856.
21. **Strand, C. L., R. R. Wajsbort, and K. Sturmann.** 1993. Effect of iodophor vs. iodine tincture skin preparation on blood culture contamination rate. JAMA **269:**1004–1006.
22. **Thorpe, T. C., M. L. Wilson, J. E. Turner, J. L. Diguiseppi, M. Willert, S. Mirrett, and L. B. Reller.** 1990. BacT/Alert: an automated colorimetric microbial detection system. J. Clin. Microbiol. **28:**1608–1612.
23. **Towns, M. L., S. Quartey, M. P. Weinstein, L. G. Reimer, and L. B. Reller.** 1993. The clinical significance of positive blood cultures: a prospective, multicenter investigation, abstr. C-232, p. 487. *In* Abstracts of the 93rd General Meeting of the American Society for Microbiology 1993. American Society for Microbiology, Washington, D.C.
24. **Weinstein, M. P., S. Mirrett, L. G. Reimer, M. L. Wilson, S. Smith-Elekes, C. R. Chuard, K. L. Joho, and L. B. Reller.** 1995. Controlled evaluation of BacT/Alert standard aerobic and FAN aerobic blood culture bottles for detection of bacteremia and fungemia. J. Clin. Microbiol. **33:**978–981.
25. **Weinstein, M. P., S. Mirrett, M. L. Wilson, L. J. Harrell, C. W. Stratton, and L. B. Reller.** 1991. Controlled evaluation of BACTEC Plus 26 and Roche Septi-Chek aerobic blood culture bottles. J. Clin. Microbiol. **29:**879–882.
26. **Weinstein, M. P., L. B. Reller, J. R. Murphy, and K. A. Lichtenstein.** 1983. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. I. Laboratory and epidemiologic observations. Rev. Infect. Dis. **5:**35–53.
27. **Wilson, M. L., T. E. Davis, S. Mirrett, J. Reynolds, D. Fuller, S. D. Allen, K. K. Flint, F. Koontz, and L. B. Reller.** 1993. Controlled comparison of the BACTEC high-blood-volume fungal medium, BACTEC Plus 26 aerobic blood culture bottle, and 10-milliliter Isolator blood culture system for detection of fungemia and bacteremia. J. Clin. Microbiol. **31:**865–871.
28. **Wilson, M. L., L. J. Harrell, S. Mirrett, M. P. Weinstein, C. W. Stratton, and L. B. Reller.** 1992. Controlled evaluation of BACTEC PLUS 27 and Roche Septi-Chek anaerobic blood culture bottles. J. Clin. Microbiol. **30:**63–66.
29. **Wilson, M. L., M. P. Weinstein, S. Mirrett, L. G. Reimer, and L. B. Reller.** 1992. Controlled comparison of the BacT/Alert and BACTEC 660/730 nonradiometric blood culture systems. J. Clin. Microbiol. **30:**323–329.
30. **Wilson, M. L., M. P. Weinstein, L. Reimer, S. Mirrett, and L. B. Reller.** 1995. Controlled evaluation of BacT/Alert anaerobic standard and FAN anaerobic blood culture bottles for the detection of bacteremia and fungemia. J. Clin. Microbiol. **33:**2265–2270.
31. **Wright, A. J., R. L. Thompson, C. A. McLimans, W. R. Wilson, and J. A. Washington.** 1982. The antimicrobial removal device: a microbiological and clinical evaluation. Am. J. Clin. Pathol. **78:**173–177.