Controlled Clinical Comparison of BacT/Alert FA Plus and FN Plus Blood Culture Media with BacT/Alert FA and FN Blood Culture Media

T. J. Kirn,^a S. Mirrett,^b L. B. Reller,^b M. P. Weinstein^a

Rutgers Robert Wood Johnson Medical School, New Brunswick, New Jersey, USA^a; Duke University Medical Center, Durham, North Carolina, USA^b

New blood culture media containing antibiotic-binding polymeric beads have been developed for the BacT/Alert (bioMérieux, Inc., Durham, NC) blood culture system. To assess the performance of these new media, we compared the new BacT/Alert aerobic medium (FA Plus) with resins to BacT/Alert FA medium with activated charcoal and the new BacT/Alert anaerobic medium (FN Plus) to BacT/Alert FN medium at 3 tertiary care medical centers. Study bottle pairs were inoculated with a target volume of 6 to 10 ml of blood from adults and incubated in the BacT/Alert 3D blood culture instrument. In the FA Plus versus FA comparison, there were 1,507 study pairs. Among 170 isolates causing true bloodstream infections (BSIs), significantly more *Staphylococcus aureus* ($P < 0.001$) and total microorganisms ($P < 0.01$) grew in the FA Plus bottle than in the FA bottle. Fewer coagulase-negative staphylococcal (CoNS) contaminants grew in the FA Plus bottle than in the FA bottle (10 versus 22; $P = 0.05$). In addition, growth was detected earlier in the FA Plus bottle than in the FA bottle ($P < 0.001$). In the FN Plus versus FN comparison, there were 2,386 study pairs. Among 201 isolates causing true BSIs, significantly more *S. aureus* ($P < 0.001$), CoNS ($P < 0.005$), and total microorganisms ($P < 0.001$) grew in the FN Plus bottle than in the FN bottle. Also, significantly more CoNS contaminants grew in the FN Plus bottle than in the FN bottle ($P < 0.001$). Overall, microorganisms were detected earlier in the FN Plus than in the FN bottle ($P < 0.001$). Medical technologists at all 3 study sites preferred the new media for Gram stain interpretation. We conclude that the FA Plus and FN Plus media provide improved and earlier detection of microorganisms compared with the FA and FN media and are preferable for Gram stain interpretation as well.

The prompt detection of bacteremia and fungemia is a critical function of the clinical microbiology laboratory. Automated systems now in use incubate blood culture specimens and signal when growth is detected. For each of these systems, different formulations of blood culture media are available. These media often contain resins or charcoal particles intended to adsorb antimicrobial agents or other substances inhibitory to bacterial growth that may be present in patient blood specimens (1). Previous studies have shown greater yields of some organisms and sometimes faster recovery of some species from such bottles than from bottles that do not contain these agents (2–6). Additionally, more recent *in vitro* and clinical studies have demonstrated an advantage of Bactec resin-containing media (BD Diagnostics, Sparks, MD) over BacT/Alert charcoal-containing media (bioMérieux, Inc., Durham, NC) (7, 8). In the present study, the clinical performance of BacT/Alert FA and FN media, which contain a proprietary charcoal-based additive, was compared to that of BacT/Alert FA Plus and FN Plus media, which contain a newly developed polymeric resin. The study was conducted at 3 geographically separate medical centers with specimens collected from adult patients suspected of having bacteremia and/or fungemia. This represents the first direct clinical comparison of BacT/Alert resin-containing media to BacT/Alert charcoal-containing media.

MATERIALS AND METHODS

Blood culture and collection. Blood specimens for culture were collected from adult patients suspected of having bacteremia or fungemia hospitalized at Duke University Medical Center (Durham, NC), Geisinger Medical Center (Danville, PA), and Robert Wood Johnson University Hospital (New Brunswick, NJ). Institutional review board approval was obtained at each study site prior to beginning the study. All specimens were collected when clinically indicated as part of routine care. Venipuncture sites

were disinfected with alcohol followed by either povidone-iodine, 2% tincture of iodine, or chlorhexidine and allowed to dry. Up to 30 ml of blood was obtained from each patient. Up to 10 ml of blood was inoculated into each of three blood culture bottles, with the study bottle (FA Plus or FN Plus) filled last. The FA Plus/FA and FN Plus/FN comparisons were performed during separate time periods; the FA Plus/FA comparison was performed first, followed by the FN Plus/FN comparison.

Study bottle pairs (FA Plus/FA or FN Plus/FN) were inoculated with 6 to 10 ml of blood from adult patients judged to have an indication for blood culture by their physician. Upon receipt in the laboratory, bottles were accessioned, assessed for blood volume adequacy, and placed into the BacT/Alert 3D blood culture instrument. Bottles were incubated for 5 days or until they signaled positive for growth. Signal-positive bottles were handled according to standard laboratory protocols for identification of microorganisms and susceptibility testing. A terminal blind subculture was performed on each signal-negative FA Plus bottle and on a subset (41.6%) of signal-negative FN Plus bottles after 5 days of incubation.

Clinical assessment. Each positive culture was reviewed and categorized as true positive, a contaminant, or an isolate of unknown clinical significance by one of the investigators at each institution. Criteria used to make these assessments were previously described (9). True positives were defined as microorganisms that are considered pathogens when isolated

Received 8 November 2013 Returned for modification 22 November 2013

Accepted 20 December 2013

Published ahead of print 26 December 2013

Editor: G. V. Doern

Address correspondence to T. J. Kirn, KIRNTJ@Rutgers.edu.

Copyright © 2014, American Society for Microbiology. All Rights Reserved.

doi:10.1128/JCM.03063-13

TABLE 1 Comparative yields of clinically important microorganisms in FA Plus and FA blood culture bottles

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FA Plus and BacT/Alert FA	BacT/Alert FA Plus only	BacT/Alert FA only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	24	23	4	<0.001
Coagulase-negative staphylococci	4	0	0	NS ^a
<i>Streptococcus</i>	27	10	3	NS
Other Gram-positive bacteria	0	0	1	NS
Gram-negative bacilli				
<i>Enterobacteriaceae</i>	24	7	6	NS
Nonfermentative Gram-negative bacilli	6	2	4	NS
Other Gram-negative bacteria	1	0	0	NS
Anaerobic bacteria	2	0	0	NS
Other fastidious bacteria	2	0	0	NS
Fungi	12	3	5	NS
All microorganisms	102	45	23	<0.01

^a NS, not significant.

from patients with signs and symptoms of disease or potential pathogens that were isolated from multiple blood cultures within a 48-h period. Contaminants were defined as (i) a single positive culture of a microorganism that is usually considered a contaminant in the absence of a possible source (e.g., a coagulase-negative staphylococcus [CoNS] isolated from a febrile patient without a central venous catheter), (ii) a single positive culture of a microorganism that is usually considered a contaminant when there is a plausible source (e.g., a central venous catheter) but that is from a clinically well patient, or (iii) a single positive culture of a single microorganism that is usually considered a contaminant when several other cultures performed within the same time frame are negative. Isolates of unknown significance were defined as (i) a single culture of a potential pathogen (e.g., coagulase-negative staphylococci, viridans group streptococci, or enterococci) from a symptomatic patient for which there is a plausible source but only one sample was submitted to the laboratory or (ii) a single culture positive for a usual contaminant (e.g., *Bacillus* spp., *Lactobacillus* spp., a diphtheroid, or *Micrococcus* spp.) in a sample from a symptomatic patient for which there was a plausible source but only one specimen was submitted to the laboratory. Patients were considered to be on antimicrobial therapy at the time of the blood collection if they were receiving an antimicrobial agent with *in vivo* activity against the microorganism isolated. This determination was based on the results of susceptibility testing performed according to CLSI guidelines or, for those isolates not ordinarily tested, the predicted susceptibility of the isolated organism.

Statistical analysis. Blood culture sets in which each bottle was filled with 6 to 10 ml of blood and in which the blood volume of the bottle with the smallest volume was within 30% of that of the bottle with the highest volume (compliant sets) were included in the analysis of the data. Comparisons of recovery rates for the bottles were done using McNemar's asymptotic chi-square test. Analysis of the time-to-detection data was performed by evaluating the differences between paired observations rather than treating each group as independent samples. The median of the differences in time to detection was evaluated using a signed-rank test, since the data were not normally distributed. A *P* value of ≤ 0.05 was considered significant.

TABLE 2 Comparative yields of clinically important microorganisms in FA Plus and FA blood culture bottles containing samples from patients receiving antimicrobial therapy

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FA Plus and BacT/Alert FA	BacT/Alert FA Plus only	BacT/Alert FA only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	7	21	3	<0.001
Coagulase-negative staphylococci	1	0	0	NS ^a
<i>Streptococcus</i>	21	8	3	NS
Gram-negative bacilli				
<i>Enterobacteriaceae</i>	17	5	2	NS
Nonfermentative Gram-negative bacilli	2	2	1	NS
Other Gram-negative bacteria	1	0	0	NS
Anaerobic bacteria	2	0	0	NS
Fungi	11	3	5	NS
All microorganisms	62	39	14	NS

^a NS, not significant.

RESULTS

In the FA Plus versus FA comparison, there were 2,444 total study pairs collected at the three institutions; 1,507 (61.6%) of these were judged to be compliant and thus included in the data analysis. Of these 1,507 compliant aerobic bottle pairs, there were a total of 219 bottle pairs that recovered at least one isolate. Of these 219 bottle pairs, 196 bottle pairs recovered a single isolate, 18 bottle pairs recovered 2 isolates, and 5 bottle pairs recovered 3 isolates. A total of 247 isolates were recovered and consisted of 170 clinically significant isolates, 61 contaminant isolates, and 16 isolates that were not classified as significant or contaminant. Of the 170 clinically significant isolates, 85 isolates were recovered from bottle pairs where both FA Plus and FA bottles were positive and recovered a single isolate. Of the 61 contaminant isolates, 12 isolates were recovered from bottle pairs where both FA Plus and FA bottles were positive and recovered a single isolate.

Among 170 isolates causing true bloodstream infections (BSIs), 102 (including those recovered as part of a polymicrobial culture) were recovered in both the FA Plus and FA bottles, 45 were recovered in the FA Plus bottles only, and 23 were recovered in the FA bottles only. Significantly more *Staphylococcus aureus* ($P < 0.001$) and total microorganisms ($P < 0.01$) grew in the FA Plus bottle than in the FA bottle (Table 1). Of 115 isolates recovered from patients on antimicrobial therapy, 62 were recovered from both FA Plus and FA bottles, 39 were recovered from FA Plus bottles only, and 14 were recovered from FA bottles only (Table 2). A statistically significantly greater number of *S. aureus* isolates was recovered from the FA Plus bottles than the FA bottles ($P < 0.001$). Among isolates judged to be contaminants ($n = 61$), fewer CoNS contaminants grew in the FA Plus bottle than in the FA bottle (10 versus 22; $P = 0.05$; Table 3). Of 85 signal-positive, clinically important microorganisms recovered from blood culture bottles growing only one organism, growth was detected earlier in the FA Plus bottle than in the FA bottle ($P < 0.001$; Table 4), where the median of the differences in time to detection was 1.4 h earlier in the FA Plus bottles than the FA bottles. Subset analysis

TABLE 3 Comparative yields of contaminant microorganisms in FA Plus and FA blood culture bottles

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FA Plus and BacT/Alert FA	BacT/Alert FA Plus only	BacT/Alert FA only	
Gram-positive cocci				
Coagulase-negative staphylococci	15	10	22	NS ^a
<i>Streptococcus</i>	1	3	1	NS
Other Gram-positive organisms	1	3	4	0.05
Fastidious organisms	0	1	0	NS
All contaminants	17	17	27	NS

^a NS, not significant.

revealed statistically significant median differences in time to detection for *S. aureus* ($P = 0.001$; median of differences, -1.5 h), streptococci ($P = 0.001$; median of differences, -1.4 h), and *Enterobacteriaceae* ($P < 0.05$; median of differences, -0.7 h). In each case, the microorganisms were detected earlier in the FA Plus bottles than in the FA bottles.

In the FN Plus versus FN comparison, there were 3,377 study pairs collected at the three institutions; 2,386 (70.6%) of these were judged to be compliant and thus included in the data analysis study pairs. Of these 2,386 compliant anaerobic bottle pairs, there were a total of 270 bottle pairs that recovered at least one isolate. Of these 270 bottle pairs, 248 bottle pairs recovered a single isolate and 22 bottle pairs recovered 2 isolates. A total of 292 isolates were recovered and consisted of 201 clinically significant isolates, 66 contaminant isolates, and 25 isolates that were not classified as significant or contaminant. Of the 201 clinically significant isolates, 107 isolates were recovered from bottle pairs where both FN Plus and FN bottles were positive and recovered a single isolate. Of the 66 contaminant isolates, 14 isolates were recovered from bottle pairs where both FN Plus and FN bottles were positive and recovered a single isolate.

Among 201 isolates causing true BSIs, 125 (including those

TABLE 5 Comparative yields of clinically important microorganisms in FN Plus and FN blood culture bottles

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FN Plus and BacT/Alert FN	BacT/Alert FN Plus only	BacT/Alert FN only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	39	21	1	<0.001
Coagulase-negative staphylococci	22	13	1	<0.005
<i>Streptococcus</i>	26	10	4	NS ^a
Other Gram-positive bacteria	2	2	0	NS
Gram-negative bacilli				
<i>Enterobacteriaceae</i>	31	13	7	NS
Nonfermentative Gram-negative bacilli	2	3	0	NS
Anaerobic bacteria	3	1	0	NS
All microorganisms	125	63	13	<0.001

^a NS, not significant.

recovered as part of a polymicrobial culture) were recovered in both the FN Plus and FN bottles, 63 were recovered in the FN Plus bottles only, and 13 were recovered in the FN bottles only. Significantly more *S. aureus* ($P < 0.001$), CoNS ($P < 0.005$), and total microorganisms ($P < 0.001$) grew in the FN Plus bottle than the FN bottle (Table 5). Of 121 isolates recovered from patients on antimicrobial therapy, 71 were recovered from both FN Plus and FN bottles, 43 were recovered from FN Plus bottles only, and 7 were recovered from FN bottles only (Table 6). A statistically significantly greater number of *S. aureus* ($P < 0.005$), CoNS ($P < 0.001$), and total microorganisms ($P < 0.001$) were recovered from the FN Plus bottles than the FN bottles (Table 6). Among isolates judged to be contaminants ($n = 66$), significantly more CoNS ($P < 0.001$) and total isolates ($P < 0.001$) grew in the FN Plus bottle than in the FN bottle (Table 7). Of 107 signal-positive,

TABLE 4 Comparative time to detection in FA Plus and FA blood culture bottles

Microorganism(s)	No. of isolates detected	Time to detection (h)				Median of differences between bottle pairs (FA Plus-FA)	P value ^a
		FA Plus bottles		FA bottles			
		Median	Range	Median	Range		
Gram-positive cocci							
<i>Staphylococcus aureus</i>	24	13.8	3.9–32.9	18.4	6.7–48.0	−1.5	0.001
Coagulase-negative staphylococci	3	21.3	16.6–22.3	25.1	22.8–29.8	−8.5	NS
<i>Streptococcus</i>	21	14.4	4.1–26.2	15.8	4.6–42.2	−1.4	0.001
Gram-negative bacilli							
<i>Enterobacteriaceae</i>	16	11.4	7.5–17.2	11.9	8.3–67.2	−0.7	<0.05
Nonfermentative Gram-negative bacilli	6	17.7	4.5–28.2	18.7	6.0–21.2	0.6	NS
Other Gram-negative bacteria							
Anaerobic bacteria	2	15.2	14.9–15.5	30.4	28.0–32.7	−15.2	NS
Other fastidious bacteria	2	12.9	12.8–13.0	14.6	14.5–14.7	−1.7	NS
Fungi	11	29.7	11.5–81.6	41.4	14.3–93.6	−2.3	NS
All microorganisms	85	14.4	3.9–81.6	16.4	4.6–93.6	−1.4	<0.001

^a P values were determined by the signed-rank test. NS, not significant.

TABLE 6 Comparative yields of clinically important microorganisms in FN Plus and FN blood culture bottles containing samples from patients receiving antimicrobial therapy

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FN Plus and BacT/Alert FN	BacT/Alert FN Plus only	BacT/Alert FN only	
Gram-positive cocci				
<i>Staphylococcus aureus</i>	16	12	0	<0.005
Coagulase-negative staphylococci	15	13	0	<0.001
<i>Streptococcus</i>	19	7	3	NS ^a
Other Gram-positive bacteria	2	0	0	NS
Gram-negative bacilli				
Enterobacteriaceae	16	9	4	NS
Nonfermentative Gram-negative bacilli	2	1	0	NS
Anaerobic bacteria	1	1	0	NS
All microorganisms	71	43	7	<0.001

^a NS, not significant.

clinically important microorganisms recovered from blood culture bottles growing only one organism, growth was detected earlier in the FN Plus bottles than in the FN bottles ($P < 0.005$; Table 8), with a median of differences in time to detection of -0.8 h. Subset analysis revealed statistically significant differences in time to detection for *S. aureus* ($P = 0.005$, -1.6 h), CoNS ($P < 0.001$, -2.9 h), and streptococci ($P < 0.05$, -0.9 h). In each case, the microorganisms were detected earlier in the FN Plus bottles than the FN bottles.

DISCUSSION

The results of this study demonstrate the superiority of the BacT/Alert FA Plus and FN Plus resin bottles to the BacT/Alert FA and FN bottles for recovery of Gram-positive bacterial etiologies of BSI. Not only did the FA Plus and FN Plus media recover more Gram-positive bacteria, but the time to detection was also improved compared with that for the charcoal-based media. Fewer Gram-negative isolates than Gram-positive isolates were recovered, but a trend was observed for improved Gram-negative bacterial recovery in the FA Plus and FN Plus media compared with the FA and FN media, respectively. A statistically significant reduction in the time to detection of Gram-negative bacteria was observed only for the FA Plus media compared with the FA media.

The use of resin beads in blood culture medium formulations has been employed by other blood culture medium manufacturers, most notably, BD, which manufactures Bactec Plus bottles. Early studies comparing the performance of such medium formulations to that of charcoal-based formulations, such as BacT/Alert FAN, did not demonstrate a significant difference between these medium types for recovery of bacteria or fungi or the time to detection of such organisms (1, 2, 10). More recently, however, both *in vitro* and clinical studies that show the superiority of resin-based media over charcoal-based media have been published (7, 8, 11). The *in vitro* studies have focused on the recovery of microorganisms from simulated blood cultures containing therapeutic levels of antimicrobials. In such studies, the superiority of Bactec Plus media compared with the BacT/Alert FA media was observed for either time to detection or frequency of recovery of the organisms tested (7, 11). A recent clinical study which included 831 positive blood cultures demonstrated a statistically significant decrease in time to detection and increased bacterial recovery for the

TABLE 7 Comparative yields of contaminant microorganisms in FN Plus and FN blood culture bottles

Microorganism(s)	No. of isolates detected in:			P value
	BacT/Alert FN Plus and BacT/Alert FN	BacT/Alert FN Plus only	BacT/Alert FN only	
Gram-positive cocci				
Coagulase-negative staphylococci	12	33	10	<0.001
<i>Streptococcus</i>	2	0	1	NS ^a
Other Gram-positive organisms	2	2	1	NS
Anaerobes	1	2	0	NS
All contaminants	17	37	12	<0.001

^a NS, not significant.

Bactec Plus aerobic media compared to those for BacT/Alert FA media (8). Factors contributing to this finding may include differences in clinical study design compared to that of prior studies, changes in antimicrobial utilization trends, differences in antimicrobial susceptibility patterns, differences in patient populations, and/or changes in medium formulations and manufacturing processes (8). Taking the *in vitro* and clinical data together, one may be inclined to conclude that the difference in performance of the medium types is most likely related to the relative ability of the additives to remove antimicrobial agents from the blood specimen.

Notably, our study demonstrated improved performance characteristics of the BacT/Alert FA Plus and FN Plus media with blood specimens collected from all patients, regardless of whether or not they were receiving antimicrobial therapy. The advantage of the resin-based media over the charcoal-based media is thus not completely explained by the presumed ability of the resin to more effectively sequester antimicrobial agents. We hypothesize that the superior performance of the FA Plus/FN Plus media may be related to other changes in medium formulation and/or the ability of the resin beads to more effectively sequester or inactivate toxic compounds other than antibiotics alone in the blood specimens.

In the FA Plus/FA comparison, we were surprised to observe that fewer CoNS judged to be contaminants grew in the FA Plus bottles than the FA bottles. This was primarily observed at one study site (Robert Wood Johnson University Hospital), and the difference just met the criteria for statistical significance ($P = 0.05$). This finding may be a result of bias associated with filling the study bottle last at the time of specimen collection. However, a similar trend was not observed in the FN Plus/FN comparison, where more CoNS and total contaminants grew in the FN Plus media than the FN media. Additional studies would be required to confirm and further explore these observations.

Due to the small number of fungi and anaerobes isolated during the course of this study, we cannot make conclusions regarding the relative performance of the new resin-containing FA Plus/FN Plus media for these organisms. Additionally, while trends suggesting improved recovery of Gram-negative bacteria were observed, too few isolates were recovered for definitive conclusions. Additional studies addressing these limitations are warranted.

An informal poll of microbiology technologists involved in this study disclosed that the overwhelming majority of them subjectively preferred the resin bottles to the charcoal bottles (both aerobic and anaerobic) because the interpretation of Gram stains was easier with the resin bottles. Many technologists commented that

TABLE 8 Comparative time to detection in FN Plus and FN blood culture bottles

Microorganism(s)	No. of isolates detected	Time to detection (h)				Median of differences between bottle pairs (FN Plus-FN)	P value ^a
		FN Plus bottles		FN bottles			
		Median	Range	Median	Range		
Gram-positive cocci							
<i>Staphylococcus aureus</i>	36	16.5	8.3–45.2	18.4	9.3–110.4	−1.6	<0.005
Coagulase-negative staphylococci	17	19.7	12.5–24.8	23.8	12.8–62.4	−2.9	<0.001
<i>Streptococcus</i>	20	13.8	6.7–84.0	13.8	8.0–100.8	−0.9	<0.05
Other Gram-positive bacteria	2	19.8	19.3–20.2	20.1	20.1–20.1	−0.4	NS
Gram-negative bacilli							
<i>Enterobacteriaceae</i>	27	11	4.6–19.2	11.6	3.8–100.8	0.0	NS
Nonfermentative Gram-negative bacilli	2	36.2	35.6–36.7	47.9	23.8–72.0	−11.8	NS
Anaerobic bacteria	3	22.3	17.7–44.6	19	17.4–19.8	3.3	NS
All microorganisms	107	15.1	4.6–84.0	17.5	3.8–110.4	−0.8	<0.005

^a P values were determined by the signed-rank test. NS, not significant.

the charcoal in the FA and FN media made it more difficult to distinguish microorganisms from medium additives. Although not specifically addressed systematically in this study, we feel that this represents another important advantage of the FA/FN Plus over the FA/FN media.

ACKNOWLEDGMENTS

We thank Paul Bourbeau for contributing data from the Geisinger Medical Center study site for inclusion in this report.

bioMérieux provided reagents and funding for this study, participated in study design, data collection, and analysis, and was permitted to review and comment on the manuscript prior to submission.

REFERENCES

- Jorgensen JH, Mirrett S, McDonald LC, Murray PR, Weinstein MP, Fune J, Trippy CW, Masterson M, Reller LB. 1997. Controlled clinical laboratory comparison of BACTEC plus Aerobic/F resin medium with BacT/ALERT aerobic FAN medium for detection of bacteremia and fungemia. *J. Clin. Microbiol.* 35:53–58.
- Pohlman JK, Kirkley BA, Easley KA, Basille BA, Washington JA. 1995. Controlled clinical evaluation of BACTEC Plus Aerobic/F and BacT/ALERT Aerobic FAN bottles for detection of bloodstream infections. *J. Clin. Microbiol.* 33:2856–2858.
- Weinstein MP, Mirrett S, Reimer LG, Wilson ML, Smith-Elekes S, Chuard CR, Joho KL, Reller LB. 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.
- Weinstein MP, Mirrett S, Wilson ML, Harrell LJ, Stratton CW, Reller LB. 1991. Controlled evaluation of BACTEC Plus 26 and Roche Septi-Chek aerobic blood culture bottles. *J. Clin. Microbiol.* 29:879–882.
- Wilson ML, Harrell LJ, Mirrett S, Weinstein MP, Stratton CW, Reller LB. 1992. Controlled evaluation of BACTEC PLUS 27 and Roche Septi-Chek anaerobic blood culture bottles. *J. Clin. Microbiol.* 30:63–66.
- Wilson ML, Weinstein MP, Mirrett S, Reimer LG, Feldman RJ, Chuard CR, Reller LB. 1995. Controlled evaluation of BacT/ALERT standard anaerobic and FAN anaerobic blood culture bottles for the detection of bacteremia and fungemia. *J. Clin. Microbiol.* 33:2265–2270.
- Flayhart D, Borek AP, Wakefield T, Dick J, Carroll KC. 2007. Comparison of BACTEC PLUS blood culture media to BacT/ALERT FA blood culture media for detection of bacterial pathogens in samples containing therapeutic levels of antibiotics. *J. Clin. Microbiol.* 45:816–821. <http://dx.doi.org/10.1128/JCM.02064-06>.
- Zadroga R, Williams DN, Gottschall R, Hanson K, Nordberg V, Deike M, Kuskowski M, Carlson L, Nicolau DP, Sutherland C, Hansen GT. 2013. Comparison of 2 blood culture media shows significant differences in bacterial recovery for patients on antimicrobial therapy. *Clin. Infect. Dis.* 56:790–797. <http://dx.doi.org/10.1093/cid/cis1021>.
- Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. 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.
- Ziegler R, Johnscher I, Martus P, Lenhardt D, Just HM. 1998. Controlled clinical laboratory comparison of two supplemented aerobic and anaerobic media used in automated blood culture systems to detect bloodstream infections. *J. Clin. Microbiol.* 36:657–661.
- Vigano EF, Vasconi E, Agrappi C, Clerici P, Melloni P. 2004. Use of simulated blood cultures for antibiotic effect on time to detection of the two blood culture systems BacT/ALERT and BACTEC 9240. *New Microbiol.* 27:235–248.