

Clinical Evaluation of BacT/Alert FA Plus and FN Plus Bottles Compared with Standard Bottles

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The performance of the BacT/Alert FA Plus and FN Plus resin bottles was evaluated in comparison with that of standard aerobic (SA) and standard anaerobic (SN) bottles. Twenty milliliters of blood from adult patients was equally distributed into four types of bottles: FA Plus, FN Plus, SA, and SN. The detection of clinically significant organisms and the time to detection (TTD) were monitored for each bottle. Among the 3,103 blood culture sets that were requested, the blood volume of each bottle was over 4 ml in 1,481 sets (47.7%). Among these 1,481 sets, 158 cultures grew in the FA Plus and SA bottles, and 136 grew in the FN Plus and SN bottles. Growth in only one type of bottle was more commonly observed for the FA Plus ($n = 38$) than for the SA ($n = 14$) ($P = 0.001$) bottles and for the FN Plus ($n = 27$) than for the SN ($n = 10$) ($P = 0.008$) bottles. Gram-negative bacilli were more frequently isolated in the resin bottles ($P < 0.05$). The skin contamination rate was 1.2% in the resin bottles and the standard bottles. The mean TTD was 11.1 h in the FA Plus bottles versus 13.1 h in the SA bottles ($P < 0.001$) and 12.0 h in the FN Plus bottles versus 12.8 h in the SN bottles ($P = 0.083$). Clinically significant bacteria, including Gram-negative bacilli, were isolated more frequently from the resin bottles than from the standard bottles. Clinically significant bacteria were detected faster using the aerobic resin bottles than using the standard aerobic bottles. This finding might not be applicable to the standard-practice 10-ml protocol for each bottle because the results from using a smaller volume (5 ml) might be less pronounced.

Sepsis is a critical illness causing high morbidity and mortality, and blood culture is essential for diagnosing sepsis. Advancements in blood culture equipment and broth media have been made for several decades. Antibiotics are sometimes empirically administered to manage urgent septic conditions, even before collecting blood for a bacterial culture. Approximately 50% to 90% of inpatients are administered antibiotics at the time of blood collection for culture (1–3). The presence of these antibiotics in the culture bottle may inhibit the growth of microorganisms.

Resin-based media are known to absorb antibiotics present in blood culture media, which is useful for the evaluation of sepsis patients who have already received antibiotics. Charcoal-based media have the same effect but might hinder the microscopic observation of Gram staining. These bottles are known to enhance the detection of microorganisms, even for sepsis patients who do not receive antibiotics, possibly by inhibiting the activities of antibodies, complement factors, or cytokines (4).

We evaluated the resin-based media that were recently developed by bioMérieux Inc. (Durham, NC), namely, FA Plus and FN Plus, for patients who visited the emergency department (ED) or who were admitted to the cancer center, the surgical intensive care unit (SICU), or the medical intensive care unit (MICU).

The early detection of microorganisms might be correlated with a better prognosis for sepsis patients (5). The time to detection (TTD) or the time to positivity is an important parameter to determine the performance of an automated blood culture system that includes blood culture bottles. We evaluated the TTD and the capability of detection of microorganisms in resin bottles compared with standard bottles produced by bioMérieux Inc.

MATERIALS AND METHODS

Patients and phlebotomy. The study population included all the adult patients (≥ 18 years old) referred for blood culture who visited the ED

($n = 1,188$) or who were admitted to the cancer center ($n = 205$), the SICU ($n = 109$), or the MICU ($n = 45$) during the study period. In total, 2,376 sets, 419 sets, 219 sets, and 89 sets were received from each department, respectively.

We informed the phlebotomists or intern physicians regarding the requirements for skin disinfection and the amount of blood to be collected before and during the study period. When a blood culture was requested, the antecubital area and bottle caps were carefully scrubbed with 0.5% chlorhexidine–alcohol. Twenty-milliliter blood samples were obtained percutaneously for each set. The blood was drawn into a syringe and distributed from the syringe into the culture bottles in random order. The collected blood was evenly divided into standard aerobic (SA), standard anaerobic (SN), resin-aerobic (FA Plus), and resin-anaerobic (FN Plus) bottles, comprising one set. Two sets of blood culture were collected for each septic event. The weight of each bottle was measured using a scale. The blood volume was calculated based on a blood density of 1.055 g/ml. The medical records were reviewed by an infectious disease specialist to determine whether the microorganisms represented significant pathogens or contaminants (6). The presence of systemic inflammatory response syndrome (SIRS), the number of culture-positive sets, the presence of intravascular catheters, the primary source of infections (such as urinary tract infections, pneumonia, or wound infections), and the growth of known skin contaminants were considered to determine the clinically significant pathogens.

The study was conducted between May and October 2012 at Gyeong-

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sang National University Hospital (GNUH) in South Korea, an 800-bed tertiary acute care university-affiliated hospital. This study was approved by the Institutional Review Board (IRB) of the hospital (GNUHIRB-2012-043). The history of antibiotic administration was retrieved from the electronic medical records (EMR) for the admitted patients or from the referring hospital by telephone for the patients who were transferred to the ED.

Blood culture procedures and microbiological analysis. The blood was cultured using a BacT/Alert three-dimensional (3D) (bioMérieux Inc.; here 3D) automated blood culture system. Each blood culture consisted of a set of four (FA Plus aerobic, FN Plus anaerobic, SA, and SN) bottles. The rate of positive blood cultures and the TTD comprised the primary endpoint. The growth of skin contaminants was monitored. The TTD was defined as the time period from the insertion of the bottles into the instrument to the detection of microorganisms. The microbiological laboratory is open from 9 a.m. to 6 p.m., and the bottles arriving at other times were stored at room temperature according to the manufacturer's recommendation. The bottles showing a positive signal in the 3D were subjected routinely to Gram staining and growth on blood agar plates, MacConkey agar plates, and chocolate agar plates. The plates were incubated overnight at 37°C with 5% CO₂. An anaerobic culture was selectively performed for the presence of organisms by Gram stain, but there was no growth in the aerobic culture; if there was growth, it occurred only in an anaerobic bottle. The colonies were identified with the Vitek system (bioMérieux Inc.). A false positive was defined as the lack of detection or growth of microorganisms with a positive signal in the 3D system.

Statistical analysis. The statistical significance was evaluated for the differences in the rate of detection of microorganisms or the rate of contamination between the FA Plus and the SA bottles and between the FN Plus and the SN bottles by the χ^2 test using exact binomial probability calculations as described by McNemar. The assumption of normality of the TTD was examined by the Kolmogorov-Smirnov test. In the cases in which the TTD data met the assumption of normality, a paired *t* test was used to test the mean TTD difference. Otherwise, we used a Wilcoxon signed-rank test. All the statistical analyses were performed using SPSS, version 20 (IBM Corp., Armonk, NY). A *P* value of < 0.05 indicated statistical significance.

RESULTS

Blood volume collected. During a 6-month period, 3,103 sets of blood cultures were requested from the ED, cancer center, SICU, and MICU. The mean (\pm standard deviation [SD]) blood volumes of the FA Plus, SA, FN Plus, and SN bottles were 4.81 (\pm 1.35) ml, 5.21 (\pm 1.25) ml, 4.83 (\pm 1.61) ml, and 4.92 (\pm 1.19) ml, respectively; the numbers of samples for each bottle type that did not reach 4 ml were 1,019 (32.8%), 405 (13.0%), 879 (28.3%), and 547 (17.6%), respectively. We excluded the data of these partially filled blood culture bottles because lower blood volume might affect the growth of organisms. A total of 1,481 (47.7%) sets that met the criteria of 4 ml were analyzed.

Microorganism detection in the FA Plus versus the SA bottles. The primary analysis was to compare the levels of effectiveness in the detection of clinically significant microorganisms of the FA Plus and SA bottles. Among the 1,481 sets analyzed, 106 (7.2%) isolates grew in both bottle types, whereas 38 (2.6%) grew only in the FA Plus bottles and 14 (1.0%) grew only in the SA bottles (Table 1). The positive rate was 10.7% (158/1,481) in the aerobic bottles. Species of gram-negative bacilli (GNB) (27 versus 13), including *Escherichia coli*, were isolated significantly more frequently from the FA bottles (*P* = 0.038) than from the SA bottles (18 versus 5) (*P* = 0.011). All the microorganisms that grew only in the FA Plus bottles (*n* = 38) were significantly more frequently isolated than in the SA bottles (*n* = 14) (*P* = 0.001).

TABLE 1 The clinically significant microorganisms isolated from the FA Plus and standard aerobic bottles^a

Microorganism(s)	No. of isolates from indicated bottle type(s)			<i>P</i> value
	Both	FA Plus only	SA only	
Gram positive	29	10	13	0.678
<i>Staphylococcus aureus</i>	6	2	0	0.500
CoNS	4	2	1	1.000
Streptococci ^b	9	5	0	0.063
Enterococci ^c	10	0	0	1.000
<i>Clostridium perfringens</i>	0	1	0	
Gram negative	70	27	13	0.038
<i>Escherichia coli</i>	40	18	5	0.011
<i>Klebsiella pneumoniae</i>	19	1	1	1.000
Other <i>Enterobacteriaceae</i> ^d	8	3	1	0.625
<i>Pseudomonas aeruginosa</i>	3	0	4	0.125
<i>Acinetobacter baumannii</i>	0	2	1	1.000
Other Gram negative ^e	0	1	0	
<i>Candida albicans</i>	2	0	0	1.000
<i>Candida non-albicans</i> ^f	5	0	0	1.000
<i>Aspergillus</i> spp.	0	1	0	
Total	106	38	14	0.001

^a Abbreviations: SA, standard aerobic; CoNS, coagulase-negative staphylococci.

^b Includes 2 *Streptococcus agalactiae*, 1 *Streptococcus mitis*/*Streptococcus oralis*, 1 *Streptococcus plurianimalium*, 2 *Streptococcus pneumoniae*, 2 *Streptococcus salivarius*, 2 *Streptococcus sanguinis*, and 4 viridans group streptococcal isolates.

^c Includes 2 *Enterococcus casseliflavus*, 3 *Enterococcus faecalis*, and 4 *Enterococcus faecium* isolates and 1 *Enterococcus gallinarum* isolate.

^d Includes 3 *Enterobacter aerogenes*, 3 *Enterobacter cloacae*, 2 *Morganella morganii*, 1 *Providencia rettgeri*, and 2 *Raoultella planticola* isolates and 1 *Salmonella enterica* serovar Typhi isolate.

^e Includes 1 *Haemophilus influenzae*, 1 *Moraxella*, and 2 *Sphingomonas paucimobilis* isolates.

^f Includes 1 *Candida guilliermondii*, 1 *Candida lusitanae*, and 3 *Candida tropicalis* isolates.

Antibiotics were prescribed for 137 of the 919 (14.9%) patients visiting the ED and 59 of the 77 (76.6%) inpatients prior to blood collection. Among the isolates from 196 patients who received antibiotics, 22 (11.2%) cultures grew in both the FA Plus and SA bottles, whereas 12 (6.1%) grew only in the FA Plus bottles, and 2 (1.0%) grew only in the SA bottles (*P* = 0.013, data not shown).

Microorganism detection in FN Plus versus SN. Cultures of a total of 99 samples (6.7%) grew in both the FN Plus and SN bottles, 27 (1.8%) grew in the FN Plus bottles only, and 10 (0.7%) grew in the SN bottles only (Table 2). The positive rate was 9.2% (136/1,481) in the anaerobic bottles. The GNB (22 versus 6), including *E. coli*, were significantly more frequently isolated in the FN Plus bottles than in the SN bottles (*P* < 0.004). Anaerobic GNB such as *Bacteroides fragilis*, *Prevotella oralis*, and *Prevotella melaninogenica* were isolated only in the FN Plus bottles. All the microorganisms that grew only in the FN Plus bottles (*n* = 27) were significantly more frequently isolated than in the SN bottles (*n* = 10) (*P* < 0.008).

Among the samples from the 196 patients who received antibiotics, 12 (6.1%) cultures grew in the FN Plus and SN bottles, whereas 17 (8.7%) grew only in the FN Plus bottles, and 1 (0.5%) grew only in the SN bottles (*P* < 0.001, data not shown).

Growth of skin contaminants. The skin contamination rates

TABLE 2 The clinically significant microorganisms isolated from the FN Plus and standard anaerobic bottles^a

Microorganism(s)	No. of isolates from indicated bottle type(s)			P value
	Both	FN Plus only	SN only	
Gram positive	31	4	3	1.000
<i>Staphylococcus aureus</i>	8	0	0	1.000
CoNS	1	2	0	0.500
Streptococci ^b	10	0	0	1.000
Enterococci ^c	10	1	0	1.000
Anaerobic Gram positive ^d	2	1	3	0.625
Gram negative	66	22	6	0.004
<i>Escherichia coli</i>	38	13	4	0.049
<i>Klebsiella pneumoniae</i>	17	3	2	1.000
Other <i>Enterobacteriaceae</i> ^e	10	2	0	0.500
Lactose nonfermenters ^f	1	0	0	1.000
Other Gram negative ^g	0	1	0	
Anaerobic Gram negative ^h	0	3	0	
<i>Candida non-albicans</i> ⁱ	2	1	1	1.000
Total	99	27	10	0.008

^a Abbreviations: SN, standard anaerobic; CoNS, coagulase-negative staphylococci.

^b Includes 2 *Streptococcus agalactiae*, 1 *Streptococcus mitis*/*Streptococcus oralis*, 1 *Streptococcus pluranimalium*, 2 *Streptococcus pneumoniae*, 1 *Streptococcus salivarius*, 1 *Streptococcus sanguinis*, and 2 viridans group streptococcal isolates.

^c Includes 2 *Enterococcus casseliflavus*, 3 *Enterococcus faecalis*, 4 *Enterococcus faecium*, and 2 *Enterococcus gallinarum* isolates.

^d Includes 2 *Bifidobacterium stercoris*, 1 *Clostridium clostridioforme*, 1 *Clostridium perfringens*, and 2 *Parvimonas micra* isolates.

^e Includes 3 *Enterobacter aerogenes*, 3 *Enterobacter cloacae*, 1 *Morganella morganii*, 1 *Providencia rettgeri*, and 2 *Raoultella planticola* isolates, 1 *Salmonella* group D isolate, and 1 *Salmonella enterica* serovar Typhi isolate.

^f Includes 1 *Pseudomonas aeruginosa* isolate.

^g Includes 1 *Haemophilus influenzae* isolate.

^h Includes 1 *Bacteroides fragilis*, 1 *Prevotella oralis*, and 1 *Prevotella melaninogenica* isolate.

ⁱ Includes 1 *Candida guilliermondii*, 1 *Candida lusitanae*, and 2 *Candida tropicalis* isolates.

were identical (1.2%) between the resin bottles and the standard bottles. Skin contaminants such as coagulase-negative staphylococci (CoNS), *Micrococcus* spp., *Corynebacterium* spp., and *Bacillus* spp. were isolated with various frequencies (Table 3). False positives were noted in 1 sample cultured in resin bottles, in 5 samples in standard bottles, and in 1 sample in both bottle types.

TTD in FA Plus versus SA bottles. The mean TTD was 11.1 h (95% confidence interval [CI], 10.2 to 11.9 h) in the FA Plus bottles versus 13.1 h (95% CI, 11.3 to 15.0 h) in the SA bottles for the microorganisms grown in both bottle types ($n = 104$, $P < 0.001$); the median TTD was 11.4 h versus 11.5 h, respectively (Table 4). The mean TTDs in the FA Plus bottles were shorter than those in the SA bottles regardless of the microorganisms ($P < 0.05$) except for CoNS, other Gram-positive organisms, and non-lactose-fermenting GNB. The difference in the median TTD was more prominent for the Gram-positive cocci (GPC) (11.5 h versus 13.1 h) than for the GNB (10.8 h versus 11.1 h). The mean difference in the TTD between the FA Plus and the SA bottles was 2.0 h.

TTD in FN Plus versus SN bottles. The mean TTD was 12.0 h (95% CI, 10.5 to 13.4 h) in the FN Plus bottles versus 12.8 h (95% CI, 10.7 to 14.8 h) in the SN bottles for the microorganisms grown in both bottle types ($n = 98$, $P = 0.083$); the median TTD was 10.6

TABLE 3 Growth of skin contaminants in the blood culture bottles

Microorganism(s)	No. (%) of isolates from indicated bottle type(s) ^a			P value
	Both	Resin	Standard	
Coagulase-negative staphylococcus	2	9	9	1.000
<i>Micrococcus</i> spp.	0	1	1	1.000
<i>Corynebacterium</i> spp.	0	3	3	1.000
<i>Bacillus</i> spp.	1	1	1	1.000
Total	3 (9.6)	14 (45.2)	14 (45.2)	1.000

^a The resin bottles included FA Plus and FN Plus, whereas the standard bottles included SA and SN.

h both in the FN Plus and SN bottles (Table 5). Compared to the aerobic bottles, the difference in the TTDs was not prominent in the anaerobic bottles. The mean TTD difference between the FN Plus bottles and the SN bottles was 0.8 h.

DISCUSSION

The resin bottles outperformed the standard bottles for the isolation of GNB, including *E. coli*, and total microorganisms. This pattern was similarly observed in the comparison of the FA bottles (charcoal) versus the SA bottles (7), the comparison of the FN bottles (charcoal) versus the SN bottles (8), and in the comparison involving all the bottles (4). *Staphylococcus aureus*, CoNS, and yeast were more significantly isolated in the FA (charcoal) bottles than in the SA bottles in a study by Weinstein et al. (9). Although *S. aureus* and streptococci were slightly more frequently detected in the resin bottles, a statistical significance was not noted in this study. As very few yeast isolates were cultured from either bottle type in this study, it is not possible to evaluate the performance of the new resin-containing culture bottles in the detection of yeast fungemia. A larger clinical evaluation should follow this study.

Some authors have suggested better performance by resin-containing Bactec Plus (BD Diagnostic Systems, Sparks, MD) bottles than by 3D charcoal-containing FAN bottles (3, 8, 10). Charcoal-containing FAN bottles appear to be less sensitive than BD Plus bottles, and it is difficult to interpret the Gram staining results. In addition, matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF) is becoming more frequently applied for the direct identification of blood culture-positive specimens (11), but charcoal hinders the process of MALDI-TOF. The 3D charcoal media detected more isolates than the Bactec Plus bottles in pediatric patients (12). Another study reported the superiority of FA bottles to Bactec Plus bottles in detecting *Enterobacteriaceae* and *Pseudomonas aeruginosa* (2). As we compared the 3D resin bottles to the 3D standard bottles, we might need to evaluate the performance of the 3D resin bottles versus the 3D charcoal bottles or versus the Bactec Plus bottles in future studies. Considering that the 3D standard bottles are widely used domestically and internationally, it is worth comparing these bottles in this study.

Blood volume is the most important parameter affecting the quality of a blood culture (13). We instructed the phlebotomists and intern physicians intensively with regard to this aspect, and the mean blood volume was satisfactory. As underfilled bottles might cause bias to our data, the sets that had one or multiple underfilled bottles (<4 ml) were removed from the data analysis.

TABLE 4 Comparison of time to detection of microorganisms grown in FA Plus and standard aerobic bottles^a

Microorganism(s) (<i>n</i>)	Time to detection (h) in indicated bottle type						<i>P</i> value ^b
	FA Plus			SA			
	Mean	95% CI	Median	Mean	95% CI	Median	
Gram-positive cocci (28)	11.0	9.2–12.7	11.5	13.3	10.2–16.3	13.1	<0.001
<i>Staphylococcus aureus</i> (6)	8.9	6.4–11.3	9.9	14.5	3.8–25.1	10.5	0.028
Coagulase-negative staphylococci (4)	10.9	2.4–19.3	10.7	15.0	1.7–28.2	12.5	0.068
Streptococci (8)	11.2	9.4–12.9	11.6	12.3	9.9–14.6	12.8	0.018
Other Gram-positive organisms (10)	12.5	9.3–15.6	14.5	13.4	9.8–16.9	14.4	0.169
Gram-negative bacilli (69)	10.9	10.0–11.7	10.8	12.6	10.0–15.1	11.1	<0.001
<i>Escherichia coli</i> (39)	10.6	9.5–11.6	11.2	13.1	8.8–17.3	11.3	0.011
Other <i>Enterobacteriaceae</i> (27)	10.7	9.0–12.3	10.3	11.5	9.5–13.4	10.1	0.021
Lactose nonfermenters (3)	15.0	13.8–16.1	14.5	16.5	14.8–18.1	15.7	0.109
Yeasts (7)	13.8	8.3–19.2	13.2	17.0	10.9–23.0	17.4	0.028
Total (104)	11.1	10.2–11.9	11.4	13.1	11.3–15.0	11.5	<0.001

^a Abbreviations: SA, standard aerobic; CI, confidence interval; *n*, number of isolates.

^b Statistical analysis by mean TTD.

Considering that the mean volumes of blood inoculated into the resin bottles were lower (0.4 ml for aerobic and 0.1 ml for anaerobic), the detection of microorganisms using these bottles appears to be superior to that seen with the standard bottles. Although we recommended distributing blood samples into the culture bottles in random order, a different mean blood volume in each bottle suggested that the distribution in the bottles appeared to have occurred in the following order (from greatest to least blood volume): SA, SN, FA Plus, and FN Plus. In particular, the cases excluded from the study because of inadequate blood volume were more prominent in the group composed of admitted patients. When we included all the data of the excluded cases, similar patterns were observed among the 3,103 sets as follows: for FA Plus bottles, 63 isolates (2.0%); for SA bottles, 32 isolates (1.0%); and for both bottle types, 220 isolates (7.1%) ($P = 0.002$); and for FN Plus bottles, 61 isolates (2.0%); for SN bottles, 18 isolates (0.6%); and for both bottle types, 203 isolates (6.5%) ($P < 0.001$) (data not

shown). Under this condition, GPC isolates were significantly more commonly collected from the FN Plus bottles than from the SN bottles (20 versus 3, $P < 0.01$).

In this study, 5 ml of blood was collected in each blood culture bottle. The usual practice in many locations is to collect 10 ml of blood per bottle or 20 to 30 ml of blood for each set via separate venipunctures per episode (13). The findings of the study may not be applicable in locations in which the standard practice is to collect 10 ml instead of 5 ml of blood per bottle. It is possible that the differences in the detection rates observed using a smaller blood volume might have been less pronounced if larger blood volumes had been cultured.

False positives were observed in a small number of the resin bottles and standard bottles. Our microbiology laboratory in which the cultures were performed was operational from 9 a.m. to 6 p.m. The culture bottles that arrived outside those hours were stored at room temperature until the next day. This practice does

TABLE 5 Comparison of the times to detection for the microorganisms grown in FN Plus and standard anaerobic bottles^a

Microorganism(s) (<i>n</i>)	Time to detection (h) in indicated bottle type						<i>P</i> value ^b
	FN Plus			SN			
	Mean	95% CI	Median	Mean	95% CI	Median	
Gram-positive cocci (30)	15.8	12.1–19.4	13.4	14.1	10.7–17.4	12.1	0.012
<i>Staphylococcus aureus</i> (8)	13.4	8.8–17.9	11.9	13.2	8.6–17.7	12.3	0.674
Coagulase-negative staphylococci (1)	13.6		13.6	11.5		11.5	
Streptococci (9)	14.8	8.6–20.9	12.0	12.8	8.9–16.6	12.0	0.214
Other Gram-positive organisms (12)	17.4	9.9–24.8	15.7	15.0	7.4–22.5	14.6	0.041
Gram-negative bacilli (66)	10.2	9.3–11.4	10.2	12.3	9.7–14.8	10.2	0.763
<i>Escherichia coli</i> (38)	8.9	8.1–10.4	9.8	12.2	8.5–15.8	10.3	0.640
Other <i>Enterobacteriaceae</i> (27)	10.8	9.6–13.5	10.4	12.4	8.5–16.2	9.9	0.183
Lactose nonfermenters (1)	13.3		17.4	18.4		18.4	
Yeasts (2)	15.5	13.9–17.0	15.5	14.7	11.3–18.0	14.7	0.655
Total (98)	12.0	10.5–13.4	10.6	12.8	10.7–14.8	10.6	0.083

^a Abbreviations: SN, standard anaerobic; CI, confidence interval; *n*, number of isolates.

^b Statistical analysis by mean TTD.

not conform to standard practice, as current guidelines recommend no more than a 2-h delay between collection and incubation in the culture instrument (13). Although it is helpful that the resin-containing bottles and standard bottles were handled the same way in this regard, it is possible that lengthy room temperature storage affected the outcome of the study.

In the *in vitro* experiments, resin or charcoal clearly suppressed the activities of antibiotics in the blood culture bottles (14, 15). Although one possible mechanism of resin or charcoal is the adsorption of antibiotics present in the blood culture bottles, this hypothesis remains to be confirmed. The resin may provide the organisms with more surface area to grow or lyse white blood cells (WBCs) to release phagocytized organisms (4). Incomplete removal of antibiotics by the FN charcoal was previously suggested (10).

The blood collection for blood culture should be performed before the prescription of antibiotics. Antibiotics are frequently given to the patients, especially for patients who are admitted to an intensive care unit (ICU) or hematology/oncology department (1). Our data demonstrated that the prior antibiotic prescription rates of the ED and ICU or cancer center were quite different. As we expected, there was a significant difference in the isolation rates between the resin media and the standard media when antibiotics were prescribed; the detection of microorganisms was more prominent in the anaerobic media (FN Plus versus SN bottles) than in the aerobic media (FA Plus versus SA bottles). Dilution of the antibiotic-containing blood by a large amount of broth (FA Plus bottles, 63.3 g; FN Plus bottles, 73.7 g) might play a role in the results seen with the anaerobic bottle in this respect.

Although the charcoal-containing media such as FA and FN showed a higher positive rate than the standard media, one disadvantage is the higher skin contamination rate (16). The comparison study of the Bactec Plus Anaerobic/F versus SN bottles showed the same result (8). There was no difference in the skin contamination rate between the resin bottles and the standard bottles in this study. The CLSI guidelines recommended that the optimal skin contamination rate should be less than 3% (13). The skin contamination rate in our study was as low as 1.2%, which might have resulted from the use of chlorhexidine-alcohol disinfectant and the good compliance of the phlebotomists for the blood culture procedure. Although there were more false positives reported for the Bactec Plus Aerobic/F bottles than for the FA charcoal bottles (68 versus 25) (2), the number of false positives was lower in the resin bottles than in the standard bottles (2 versus 6), and false positives were much less common in this study.

Early detection of positive samples is essential for the management of sepsis patients (5). The TTD is a good indicator for evaluating the performance of automatic blood culture machines or media. Although there was a significant difference in the mean TTDs between the FA Plus bottles and the SA bottles, the median TTDs (11.4 h versus 11.5 h) were closer than the mean TTDs (11.1 h versus 13.1 h), suggesting that there were more organisms growing slowly in the standard bottle group. The mean TTD for the FN Plus bottles was similar to that for the SN Plus bottles. The TTD for the SN bottles was shorter than that for the FN charcoal bottles in a previous study (8). We may conclude that the TTD was shorter in the FA Plus bottles than in the SA bottles but that the TTDs were equivalent for the FN Plus and SN bottles.

This study showed that clinically significant bacteria were isolated more frequently from the resin bottles than from the stan-

dard bottles, both overall and in the subgroup of patients who had received antibiotics prior to specimen collection. There was no difference in the rate of contamination between the resin-containing bottles and the standard bottles. Clinically significant bacteria were detected faster using the aerobic resin bottles than using the standard aerobic bottles.

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REFERENCES

- Kang H, Kim S. 2012. Clinical features associated with blood cultures according to the use of antimicrobial agents prior to blood collection. *Korean J. Clin. Microbiol.* 15:21–26.
- 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.
- Roh KH, Kim JY, Kim HN, Lee HJ, Sohn JW, Kim MJ, Cho Y, Kim YK, Lee CK. 2012. Evaluation of BACTEC Plus aerobic and anaerobic blood culture bottles and BacT/Alert FAN aerobic and anaerobic blood culture bottles for the detection of bacteremia in ICU patients. *Diagn. Microbiol. Infect. Dis.* 73:239–242. doi:10.1016/j.diagmicrobio.2012.03.022.
- Gibb AP, Hill B, Choresl B. 1998. Comparative study of BacT/Alert FAN bottles and standard BacT/Alert bottles. *Diagn. Microbiol. Infect. Dis.* 32:159–163.
- Barenfanger J, Graham DR, Kolluri L, Sangwan G, Lawhorn J, Drake CA, Verhulst SJ, Peterson R, Moja LB, Ertmoed MM, Moja AB, Shevlin DW, Vautrain R, Callahan CD. 2008. Decreased mortality associated with prompt Gram staining of blood cultures. *Am. J. Clin. Pathol.* 130: 870–876. doi:10.1309/AJCPVMDQU2ZJDPBL.
- Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM. 1988. CDC definitions for nosocomial infections, 1988. *Am. J. Infect. Control* 16:128–140.
- Frank U, Malkotsis D, Mlangeni D, Daschner FD. 1999. Controlled clinical comparison of three commercial blood culture systems. *Eur. J. Clin. Microbiol. Infect. Dis.* 18:248–255.
- Wilson ML, Mirrett S, Meredith FT, Weinstein MP, Scotto V, Reller LB. 2001. Controlled clinical comparison of BACTEC plus anaerobic/F to standard anaerobic/F as the anaerobic companion bottle to plus aerobic/F medium for culturing blood from adults. *J. Clin. Microbiol.* 39:983–989. doi:10.1128/JCM.39.3.983-989.2001.
- 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.
- 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. doi:10.1093/cid/cis1021.
- Lagace-Wiens PR, Adam HJ, Karlowsky JA, Nichol KA, Pang PF, Guenther J, Webb AA, Miller C, Alfa MJ. 2012. Identification of blood culture isolates directly from positive blood cultures by use of matrix-assisted laser desorption/ionization-time of flight mass spectrometry and a commercial extraction system: analysis of performance, cost, and turnaround time. *J. Clin. Microbiol.* 50:3324–3328. doi:10.1128/JCM.01479-12.
- Lee KH, Song W, Park MJ, Hyun J, Kim HS, Lee KM. 2011. Comparison of the BACTEC Peds Plus pediatric blood culture bottle to the BacT/Alert PF pediatric blood culture bottle for culturing blood from pediatric patients. *Korean J. Clin. Microbiol.* 14:126–130.
- Clinical and Laboratory Standards Institute. 2007. Principles and procedures for blood cultures; approved guideline. CLSI document M47-A. Clinical and Laboratory Standards Institute, Wayne, PA.

14. Lee JY, Hong JH, Lee M. 2010. Comparison of BACTEC Plus Aerobic/F Media and BacT/Alert FA Media to detect bacteria in blood culture bottles containing peak therapeutic levels of antimicrobials. *Korean J. Clin. Microbiol.* 13:151–156.
15. Mitteregger D, Barousch W, Nehr M, Kundi M, Zeitlinger M, Makristathis A, Hirschl AM. 2013. Neutralization of antimicrobial substances in new BacT/Alert FA and FN Plus blood culture bottles. *J. Clin. Microbiol.* 51:1534–1540. doi:10.1128/JCM.00103-13.
16. Mirrett S, Petti CA, Woods CW, Magadia R, Weinstein MP, Reller LB. 2004. Controlled clinical comparison of the BacT/ALERT FN and the standard anaerobic SN blood culture medium. *J. Clin. Microbiol.* 42: 4581–4585. doi:10.1128/JCM.42.10.4581-4585.