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Comparison of the BacT/Alert PF Pediatric FAN Blood Culture Bottle with the Standard Pediatric Blood Culture Bottle, the Pedi-BacT

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The performance of the BacT/Alert PF (Organon-Teknika Corp., Durham, N.C.), a new nonvented pediatric FAN blood culture bottle, was compared to that of the original pediatric bottle, the Pedi-BacT, with matched aerobic cultures obtained from two separate facilities. A total of 244 clinically significant isolates were recovered from 4,015 compliant pairs. Among the positive cultures, 170 (70%) isolates were detected in both the BacT/Alert PF and the Pedi-BacT bottles, while 47 (19%) isolates were recovered in the BacT/Alert PF bottle only and 27 (11%) isolates were recovered in the Pedi-BacT bottle only. Although isolation of specific microorganisms was comparable for the two bottles, the total number of organisms recovered by the BacT/Alert PF was greater than that by the Pedi-BacT ($P = 0.0272$). In addition, more organisms were recovered by the BacT/Alert PF bottle from the blood of patients receiving antimicrobial therapy ($P = 0.0180$). Overall time to detection was similar for the two bottles; however, a significantly decreased mean time to detection was recorded for yeast from the BacT/Alert PF bottle (22.9 h; $P = 0.0001$) and staphylococci from the Pedi-BacT bottle (22.5 h; $P = 0.0056$). One false-negative culture and five false-positive cultures occurred with the Pedi-BacT bottle, compared to one false-positive culture with the BacT/Alert PF bottle. The BacT/Alert PF bottle is a reliable blood culture bottle for pediatric blood culture specimens and may offer improved recovery of microbes from patients on antimicrobial therapy. The use of the nonvented bottle will both facilitate bottle processing and decrease expenditures for materials due to the elimination of the venting needles required for the original vented bottles.

The performance of blood cultures from pediatric patients poses certain challenges not experienced when performing blood cultures for adult populations. The difficulties in collection of pediatric specimens coupled with concerns regarding volume depletion affect the amount of blood available for culture (2, 3, 4). Other factors include the fastidious nature of pediatric pathogens such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, the changing venue of pathogens commonly retrieved from blood culture specimens, and the documentation of low concentrations of circulating organisms in the blood of some pediatric patients (2, 3, 4, 9). In response to these considerations, manufacturers of blood culture instruments have developed blood culture bottles for use exclusively in pediatric populations. These bottles differ from adult blood culture bottles in both formulation and volume of broth. Pediatric blood culture bottles are designed to hold approximately 20 ml of broth and accommodate an inoculation volume of up to 4 ml. Although adult blood culture bottles containing resins or charcoal-based substances for absorption of antimicrobial agents or other inhibitory substances were introduced several years ago, such additives were not available in a pediatric formulation. In the present study, the performance of the newly developed pediatric FAN blood culture bottle, the BacT/Alert PF (Organon-Teknika Corp., Durham, N.C.) was compared to the first generation of pediatric blood culture bottle produced by Organon-Teknika Corp., the Pedi-BacT, for use with their continuously monitoring blood culture system.

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MATERIALS AND METHODS

Patient population. Calgary Laboratory Services (CLS), Calgary, Canada, is a centralized regional laboratory that provides microbiology services for both adult and pediatric patient populations, including the Alberta Children's Hospital. Children's Medical Center of Dallas, Dallas, Texas, (CMC) is a tertiary care pediatric teaching hospital.

Blood culture bottles. Each bottle contains 20 ml of medium. The broth formulation of the BacT/Alert PF bottle is a casein soy base supplemented with brain heart infusion solids and other proteins with the addition of activated charcoal (8.5% wt/vol) and 0.025% sodium polyethanolesulfonate. The Pedi-BacT bottle contains a media formulation that is composed of a brain heart infusion base with .020% sodium polyethanolesulfonate. The atmosphere of the BacT/Alert PF bottle is oxygen and nitrogen, thus eliminating the need to vent the bottle. The content of the Pedi-BacT bottle is overlaid with carbon dioxide and nitrogen and requires venting prior to incubation.

Specimen collection and laboratory processing. Unless otherwise designated, the methods used by both facilities for bottle processing were equivalent as established by the investigational study protocol. Blood from a single collection site was inoculated into each set of bottles. Individuals were instructed to inoculate the Pedi-BacT bottle first to ensure the performance of culture by the reference method. The optimum collection volume was set at 4.0 ml of blood for each bottle included in the evaluation. If a total of 8 ml was not collected, the blood was divided equally between the two bottles. Standard recommended antisepsis procedures were used during blood specimen collection. Upon receipt, the bottle was visually inspected for growth, proper inoculation, and pertinent patient collection information. Only paired study bottles containing blood from the same collection sites and times were included in the study. The weight of each bottle was recorded and compared to the preinoculation bottle weight for comparison of blood inoculation volumes. Bottles were monitored for the presence of bacterial growth every 10 min by the instrument. Any growth-positive bottle was processed promptly after detection, while the corresponding bottle was not

TABLE 1. Combined yields of clinically significant (sepsis) isolates from Pedi-BacT and BacT/Alert PF bottles from both study sites

Organism group[a]	No. of isolates recovered		
	BacT/Alert PF and Pedi-BacT	BacT/Alert PF only	Pedi-BacT only
Staphylococcus aureus	21	5	1
Coagulase-negative staphylococci	33	7	4
Group A streptococci	0	2	0
Group B streptococci	2	0	0
Streptococcus pneumoniae	9	7	4
Alpha-hemolytic streptococci	11	2	0
Streptococcus milleri group	0	1	0
Enterococci	12	1	3
Enterobacteriaceae[b]	37	16	11
Miscellaneous nontermenters[c]	5	2	1
Fastidious gram-negative species[d]	2	1	1
Miscellaneous gram-positive organisms[e]	6	1	1
Candida spp.	32	2	1
Total[f]	170	47	27

[a] Includes organisms from monomicrobial and polymicrobial cultures.
[b] Includes 1 isolate of *Enterobacter agglomerans*, 19 isolates of *E. cloacae*, 1 isolate of *E. gergoviae*, 17 isolates of *Escherichia coli*, 3 isolates of *Serratia marcescens*, 18 isolates of *Klebsiella pneumoniae*, 2 isolates of *K. oxytoca*, 1 unidentified bacillus, 1 isolate of *Salmonella* group B, and 1 isolates of *Salmonella* group D.
[c] Includes 1 isolate of *Pseudomonas aeruginosa*, 1 isolate of *Pseudomonas fluorescens* group, 1 isolate of *Pseudomonas* spp. 3 isolates of *Stenotrophomonas maltophilia*, 1 of isolate of *Acinetobacter baumannii*, and 1 unidentified bacillus.
[d] Includes 3 isolates of *Haemophilus influenzae* and 1 isolate of *Neisseria meningitidis*.
[e] Includes 3 isolates of *Stomatococcus* spp., 1 isolate of *Corynebacterium* spp., 3 isolates of *Bacillus* spp., and 1 isolate of *Eubacterium limosum*.
[f] $P = 0.0272$.

processed until the bottle was recorded as positive by the BacT/Alert instrument. Subcultures and direct smears from both systems were performed at the first indication of a positive culture. Cultures that were initially indicated to be positive but did not contain bacterial growth were reincubated and monitored for the remainder of the incubation period. Terminal subcultures were performed at the completion of the 5-day incubation period in cases in which a positive culture was accompanied by a negative bottle result. Organisms were identified by established procedures for identification and susceptibility testing.

Data analysis. In addition to the culture collection date and time, pre- and postinoculation bottle weights, lot numbers, and pertinent patient information, the following data were collected in conjunction with the study: (i) receipt date and time (designated for both systems as the time when the Pedi-BacT bottles were logged into the instrument); (ii) time to a positive result (designated as the time a positive signal and/or a positive smear or culture was recorded); (iii) a false-positive result (defined as a culture that was found to be positive by the instrument or visual examination but whose positivity was not confirmed by direct smear or subculture); (iv) a false-negative result (defined as a culture found to contain growth only after terminal subculture); (v) the antimicrobial agent(s) administered to the patient during the culture collection period; and (vi) the white blood cell count. Organisms retrieved from culture were categorized as clinically significant or probable contaminants on the basis of standard recommendations (5, 10), a total white blood cell count suggestive of infection, and the administration of antimicrobial therapy. In those instances in which a category could not be assigned, the isolate was designated as category unknown.

Statistical methods. Statistical comparisons were evaluated by the chi-square test for paired data (McNemar's test with the Yates correction for small numbers of observations) (1). The significance of times to detection by each system was evaluated by the Wilcoxon signed-rank test.

TABLE 2. Combined yields of clinically insignificant isolates from Pedi-BacT and BacT/Alert PF bottles from both study sites

Organism group[a]	No. of isolates recovered		
	BacT/Alert PF and Pedi-BacT	BacT/Alert PF only	Pedi-BacT only
Yeast[b]	1	2	0
Staphylococcus aureus	0	2	0
Coagulase-negative staphylococci	19	34	27
Miscellaneous gram-positive organisms[c]	5	17	23
Fastidious gram-negative species[d]	0	3	3
Acinetobacter lwoffii	0	1	0
Total[e]	25	59	53

[a] Includes organisms from monomicrobial and polymicrobial cultures.
[b] Includes 2 *Candida albicans* isolates and 1 *Candida glabrata* isolate.
[c] Includes 11, isolates of *Corynebacterium* spp., 13 isolates of *Bacillus* spp., 1 isolate of *Enterococcus faecalis*, 1 isolate of group D enterococcus spp., 2 isolates of *Micrococcus* spp., 1 isolate of mixed gram-positive bacilli, 1 group C streptococcus, and 15 viridans group streptococci.
[d] Includes 1 isolate of *Capnocytophaga* spp., 2 isolates of *Moraxella catarrhalis*, and 3 isolates of *Neisseria* spp.
[e] $P = .6366$.

RESULTS

Collection volumes were determined by both study sites using the pre- and postinoculation weights of the paired set. Blood volumes of ≤2.5 ml were inoculated into 80 to 82% of CMC blood culture bottles and 58 to 65% of CLS blood cultures. A greater than 30% difference in inoculation volumes was recorded for more than 40% (49% for CMC and 43% for CLS) of the bottles included in the comparison. Using the previously published limit of a twofold difference between bottle volumes as the criterion for a paired set for pediatric blood cultures (12), >90% of the bottles included in the evaluation (93% for CMC and 86% for CLS) satisfied the requirement for matched volumes.

During the evaluation period, a total of 4,015 matched pairs of blood culture specimens were received for comparative analysis by both facilities. A total of 346 positive cultures were detected from 221 patients. Of these cultures, 197 monomicrobial cultures and 23 polymicrobial cultures from 113 patients were categorized as clinically significant (sepsis). Of the 244 clinically significant bacterial and fungal isolates recovered from the matched pairs of both monomicrobial and polymicrobial cultures, 170 (70%) were recovered from both systems, while 47 (19%) were recovered from the BacT/Alert system only and 27 (11%) were recovered from the Pedi-BacT bottle only (Table 1). Overall recovery of organisms was improved with the BacT/Alert PF bottle ($P = 0.0272$). No significant difference was found in the recovery of microorganisms classified as clinically insignificant (Table 2). For clinically significant cultures from patients on antimicrobial therapy, the overall rate of retrieval of isolates was higher for the BacT/Alert PF than for the Pedi-BacT bottle ($P = 0.0180$) (Table 3). The overall times to detection ranged from 3.3 to 60 h for the BacT/Alert PF bottle compared to 3.4 to 122.4 h for the Pedi-

TABLE 3. Effect of antibiotic therapy on comparative yields of clinically significant monomicrobial isolates from Pedi-BacT and BacT/Alert PF bottles at CMC and CLS

Organism group	No. of organisms recovered					
	Patients receiving antimicrobial therapy			Patients not receiving antimicrobial therapy		
	BacT/Alert PF and Pedi-BacT	BacT/Alert PF only	Pedi-BacT only	BacT/Alert PF and Pedi-BacT	BacT/Alert PF only	Pedi-BacT only
Staphylococcus aureus	10	5	0	11	0	1
Coagulase-negative staphylococci	25	4	3	1	1	0
Group A and B streptococci	1	1	0	1	1	0
Streptococcus pneumoniae	5	2	1	1	5	1
Alpha-hemolytic streptococci	6	1	0	4	2	0
Enterococci	4	0	2	0	0	1
Enterobacteriaceae[a]	11	11	2	8	3	4
Miscellaneous organisms[b]	4	0	2	5	2	1
Candida spp.	13	1	0	5	1	0
Total[c]	79	25	10	36	15	9

[a] Includes *Enterobacter agglomerans, Enterobacter gergoviae, Enterobacter cloacae, Escherichia coli, Serratia marcescens, Klebsiella pneumoniae, Klebsiella oxytoca, Salmonella* groups B and D, and an unidentified gram-negative rod.
[b] Includes *Pseudomonas aeruginosa, Stenotrophomonas maltophilia*, unidentified nonfermenter, *Haemophilus influenzae, Stomatococcus* spp., *Corynebacterium* spp., and *Bacillus* spp.
[c] Retrieval of isolates from a patient receiving antimicrobial agents in the BacT/Alert PF was statistically significant ($P = 0.0180$).

BacT bottle (Table 4). The mean time to detection for yeast was significantly decreased (22.9 h; $P = 0.0001$) with the BacT/Alert PF but was increased for staphylococcus species (20.3 h; $P = 0.0056$) compared to results with the Pedi-BacT bottle.

One false-positive culture was detected with the BacT/Alert PF bottle, and five false-positive cultures and one false-negative culture were detected with the Pedi-BacT bottle. A staphylococcus strain was isolated from the standard bottle with no resultant growth from the Pedi-BacT bottle.

DISCUSSION

The BacT/Alert pediatric blood culture bottle debuted in 1993 (6); however, a pediatric FAN bottle formulation was not available for evaluation until 1998. The present study was the first clinical comparison of the new BacT/Alert PF to the standard Pedi-BacT bottle.

The BacT/Alert PF bottle was superior to the Pedi-BacT bottle in overall detection of all microorganisms recovered during the evaluation. Although the numbers were small, im-

TABLE 4. Times to detection of clinically significant (sepsis) isolates from Pedi-BacT and BacT/Alert PF bottles from both study sites

Organism group	No. of isolates	Time to detection (h)[a]					
		BacT/Alert PF			Pedi-BacT		
		Mean	Median	Range	Mean	Median	Range
Candida spp.[b]	32	22.9	23.3	7.3–41.5	28.8	27.7	11.5–48.0
Gram-negative bacilli	25	13.2	12.0	3.3–38.5	12.8	11.5	3.4–29.7
Enterobacteriaceae	21	11.6	10.7	3.3–18.0	11.6	11.0	3.4–29.7
Fastidious gram-negative organisms	2	28.4	28.4	18.2–38.5	21.1	21.0	18.8–23.4
Glucose nonfermenters	2	15.8	15.8	13.3–18.2	16.9	16.9	16.2–17.5
Gram-positive organisms	81	19.8	14.7	4.0–60.0	17.61	13.5	5.1–122.4
Staphylococci[b]	50	22.5	18.6	8.0–60.0	20.3	14.0	7.0–122.4
Streptococci	25	13.6	13.3	4.0–24.0	12.3	12.3	5.1–20.7
Other	6	22.4	15.9	9.5–55.2	17.6	16.0	8.7–33.7
Total	138	19.3	15.2	3.3–60.0	19.3	14.3	3.4–122.4

[a] Time-to-detection data is presented for monomicrobial isolates recovered in both bottles of a paired set.
[b] Only the mean times to detection for staphylococci (earlier in Pedi/BacT; $P = 0.0056$) and yeast (earlier in BacT/Alert PF; $P = 0.0001$) were statistically significant.

portant pediatric pathogens, such as *Streptococcus pneumoniae* and *Neisseria meningitidis*, were recovered equally well by both systems; however, a comparison of the two medium formulations for significant differences in their abilities to retrieve more fastidious fermenters and nonfermenters was not possible because of the low incidence of these isolates. Yeast, however, were detected more rapidly in the new bottle.

Retrieval of isolates from patients receiving antimicrobial therapy was also significantly improved with the BacT/Alert PF. Both bottles have a different medium formulation in addition to the activated charcoal in the BacT/Alert PF bottle. Although the exact mode of action of the activated charcoal is unknown, the substance is designed to improve the retrieval of blood-borne pathogens, especially in the presence of antimicrobial agents. These assertions have been confirmed by documentation of the performance of the adult BacT/Alert FAN bottle in other published evaluations (7, 8, 11).

Questions arise concerning the advantage the BacT/Alert PF bottle might provide from a clinical perspective. In a retrospective analysis performed by McDonald et al. (7) on the clinical impact of the adult FAN bottle, the increased recovery rate for clinically important episodes of bacteremia or fungemia did positively influence therapeutic decisions and other diagnostic modalities to some degree. Such advantages would be even more important in a pediatric institution, where rapid detection of pathogens is critical to patient outcomes in many situations.

The need for a FAN bottle designed specifically for pediatric specimens, however, is debated. Many institutions maintain only an adult standard or FAN blood culture bottle for use with smaller-volume pediatric specimens. Since some infants and children maintain higher levels of circulating organisms during sepsis, the concern over larger blood-to-broth ratios is negated. Depending on the collection time, the infecting organism and/or host response, and the source of bacteremia, however, a percentage of cultures will contain lower pathogen concentrations (2, 3). Potential loss of organisms or decreased times to positivity may adversely affect clinical diagnosis and therapeutic decisions. The utilization of a pediatric FAN blood culture bottle offers the advantage of a nutritionally supplemented broth in a reduced volume conducive to the promotion of growth of most pediatric pathogens. The present evaluation confirms the overall favorable performance of the BacT/Alert PF bottle and indicates the potential for improved recovery of isolates in the presence of antimicrobial agents or other inhibitory agents. In addition, the elimination of the requirement for bottle venting will facilitate processing of the bottle in the clinical laboratory as well as resulting in cost-savings due to the elimination of venting needles.

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