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Frequency of Low-Level Bacteremia in Children from Birth to Fifteen Years of Age

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A single blood culture inoculated with a small volume of blood is still frequently being used for the diagnosis of bacteremia in children because of the continued belief by many that bacteria are usually found in high concentrations in the blood of pediatric patients with sepsis. To determine the importance of both blood volume cultured and the number of culture devices required for the reliable detection of pathogens in our pediatric population, blood from children from birth to 15 years of age and with suspected bacteremia at York Hospital (a 500-bed community hospital) was inoculated into at least a Pediatric Isolator (Wampole Laboratories; 1.5 ml of blood) or a standard Isolator (10 ml of blood) and a bottle of ESP anaerobic broth (Trek Diagnostic Systems; 0.5 to 10 ml of blood). The use of a second Isolator and additional aerobic and anaerobic bottles and the total blood volume recommended for cultures (2 to 60 ml) depended on the weight and total blood volume of each patient. One hundred forty-seven pathogens were recovered from the blood of 137 (3.6%) of 3,829 children for whom culturing was done. Of 121 septic episodes for which the concentration of pathogens in the blood could be determined using Isolators, 73 (60.3%) represented low-level bacteremia (≤10 CFU/ml of blood), including 28 pathogens (23.1%) which were detected at concentrations of only ≤1.0 CFU/ml. Of 144 septic episodes for which two or more culture devices (Isolators and/or bottles) were inoculated, 85 (59%) were associated with false-negative results from one or more of the culture devices. Of the 128 children for whom antibiotic therapy records were complete, therapy was either started or changed for 88 (68.8%) following notification of positive blood cultures. Low-level bacteremia was common in our pediatric population, requiring the culturing of up to 4 or 4.5% of a patient's total blood volume for the reliable detection of pathogens and appropriate, timely changes in empiric therapy.

In two well-documented studies, only 25 to 26% of pediatric patients who were admitted to intensive care units with clinical evidence of sepsis had blood cultures from which pathogens were recovered (16, 29). Previous studies which have based a diagnosis on a single small-volume blood culture have underestimated the prevalence of bacteremia in children (15). Blood volumes traditionally used for cultures for infants and older children are frequently inadequate for the comprehensive and rapid detection of pathogens which may be present in relatively low concentrations in the blood (15, 17, 24, 30). As little as 1 ml of blood has been routinely cultured for pediatric patients (8), and a recent report suggests that 0.2 ml of blood provided 95% sensitivity, compared to 2 ml of blood, for infants from birth to 12 months of age (32). In another recent study, only 1 to 3 ml of blood was cultured in a single aerobic bottle for children between 3 and 36 months of age and at risk for occult bacteremia (22).

Low-level bacteremia (≤10 CFU/ml) may be more common in pediatric patients than has been previously thought and has been reported in up to 38% of culture-positive children, as previously reviewed (20). Reasons for culturing small volumes of blood from pediatric patients have included concern about the small blood volumes of younger patients (11, 13, 21, 30, 31), difficulties frequently encountered in obtaining blood from children (15, 30), desires both to avoid the need for blood transfusions after repeated phlebotomies (24, 30, 31, 39) and to start antibiotics without delay (10–13, 39), and the common belief throughout the 1990s that bacterial concentrations are often greater ("far greater" [32]) in the blood of younger patients than in that of adults (26, 28, 39, 40). However, the advantages of culturing larger volumes of blood from children and inoculating two or more culture devices (bottles and/or Isolators) include an increase in the number of children from whom pathogens are detected (8, 9, 15, 17, 24, 30, 35, 39), a decrease in detection times (15, 35), an improved ability to differentiate pathogens from contaminants (1, 5, 25, 34, 37, 39), assistance either with the selection of more specific antimicrobial agents when a pathogen is detected and identified or with the discontinuation of unnecessary therapy when a sensitive blood culture system remains negative for pathogens (2, 6, 12, 14, 25, 33, 37, 38), reduction of both overall costs (6, 7, 36) and selection of resistant microorganisms (6) when empiric therapy is changed to specific therapy following the report of positive blood cultures, and additional reimbursement when pathogens are detected (4).

A recent study at York Hospital determined both that 68% of our infants up to 2 months of age had low-level bacteremia and that culturing of up to 6 ml of blood (up to 4.5% of an infant's total blood volume) was required for the detection of pathogens from those infants (19). It seems appropriate that the volume of blood cultured from a pediatric patient should directly depend on the patient's weight (and total blood volume) and age (17, 20, 27). The current study was undertaken to determine the frequency of low-level bacteremia in the York Hospital general pediatric population as well as the importance of blood volume cultured for the detection of pathogens and the impact of positive blood culture reports on appropriate changes in empiric therapy.

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TABLE 1. Blood volumes recommended for culturing at York Hospital

Patient's wt (kg)	Blood vol (ml) used for:						Maximum loss of total blood vol (%)
	Culture set 1			Culture set 2			
	Isolator	Aerobic bottle	Anaerobic bottle	Isolator	Aerobic bottle	Anaerobic bottle	
≤1	1.5		0.5				4
1.1–2	1.5		1.5	1.5			4.5
2.1–12.7	1.5		3.0	1.5			3
12.8–36.3	1.5	5.0	5.0	1.5	5.0	5.0	2.9
>36.3	10	10	10	10	10	10	2.8

MATERIALS AND METHODS

Infants and children from birth to 15 years of age and with clinical signs and symptoms of sepsis at York Hospital (a 500-bed community hospital) were included in the study. The amount of blood (2 to 60 ml) recommended for culturing from each patient depended on the weight of the patient (Table 1). Two blood cultures consisting of at least three and up to six culture devices were specified for patients weighing more than 1 kg. These recommended blood volumes were consistent with a policy for routine blood culturing which had been previously established by the hospital neonatologists, pediatricians, and microbiology laboratory (20) and represented no more than 3 to 4.5% of a patient's total blood volume and usually considerably less. Blood was collected by neonatologists, pediatricians, nurses, or phlebotomists and inoculated into either Pediatric Isolators or 10-ml standard Isolators (Wampole Laboratories, Cranbury, N.J.) as well as aerobic and/or anaerobic ESP culture bottles (Trek Diagnostic Systems, Westlake, Ohio), as shown in Table 1. In some cases, physicians collected more or less than the recommended blood volumes and submitted more or fewer than the recommended number of culture devices (Isolators and/or bottles). Blood for culturing from infants was usually collected at the same time and from the same site. Blood for culturing from older children was usually collected from different sites and 0.5 h apart. Approximately 95% of the blood samples were obtained using venipuncture. The remainder were collected from central venous lines. In most cases, the venipuncture site was decontaminated prior to blood collection by using a three-step procedure with isopropyl alcohol, povidone-iodine, and isopropyl alcohol.

Once the blood cultures were received in the laboratory, the approximate blood volume in each culture device (Isolators and bottles) was measured by comparing the volume of fluid with that in identical devices on which volume lines had been drawn. These lines represented blood volumes of 0.5, 1.0, and 1.5 ml for the Pediatric Isolators and 1-ml increments for the 10-ml Isolators and the bottles. This method of blood volume determination has been in routine use for all blood cultures in our laboratory for about 10 years. It is simple, rapid, and reasonably accurate, especially with Isolators and also with bottles containing more than 2 ml of blood. The centrifuged sediment from 10-ml Isolators and the entire specimen from Pediatric Isolators (1.5 ml) were inoculated onto two sheep blood and two chocolate agar plates exactly as specified by the Isolator manufacturer. The agar cultures were incubated for recovery of aerobic and facultatively anaerobic pathogens as previously described (18). Positive Isolator cultures were Gram stained and subcultured once daily. Colony counts of bacteria in the blood were determined from positive Isolator cultures as previously described (19), and low-level bacteremia was defined as ≤10 CFU/ml of blood (15, 19). Culture bottles were incubated for 6 days at 35°C and continuously monitored in ESP incubators. Bottles flagged as positive by the ESP system were Gram stained, subcultured, and reported as positive within 1 h of their detection, 24 h a day. Isolates of bacteria and yeasts were identified by conventional biochemical and serological methods (23).

The clinical significance of the microbial isolates was determined by one of the authors (J.P.M.) using previously published guidelines, including clinical signs and symptoms (i.e., fever, low birth weight, poor feeding, apnea, and bradycardia), laboratory findings (such as abnormal complete blood counts, species identification, number of positive blood culture devices, relative time to detection, and recovery of the same species from another body site), radiographic findings (including chest infiltrates), and predisposing factors (1, 5, 10, 12, 25, 31, 34, 38). Isolates of *Bacillus* spp., *Corynebacterium* spp., *Propionibacterium* spp., and coagulase-negative staphylococci recovered from a single culture device were considered contaminants (5, 10, 34, 35, 37). The *z* test for differences in proportions for independent samples was used for statistical analysis of results (36a). A P value of <0.05 was selected as the minimum level of significance.

RESULTS

From 1 June 1995 until 13 June 1999, blood cultures were done for 3,829 pediatric patients. The age range was newborn to 15 years (mean, 2.3 years; median, 1.0 year). Contaminants were recovered from one or more devices in 267 (3.4%) of the 7,930 cultures from these patients, including 165 (2.1%) of 7,916 Isolators, 64 (2.0%) of 3,219 aerobic bottles, and 67 (1.2%) of 5,763 anaerobic bottles. During the 4-year interval, 137 patients (or 3.6% of the total) had 140 episodes of bacteremia or fungemia involving 147 pathogens. The age range of these patients was newborn to 15 years (mean, 2.2 years; median, 0.6 year). One patient had three separate septic episodes with different pathogens over a 6-week interval, and another had two episodes, 3 months apart. Of the 137 patients with significant isolates, 82 (60%) were male and 55 (40%) were female. The mortality rate for these patients was 5.1% (7 of 137).

Although a wide variety of pathogens were recovered from the patients, *Streptococcus pneumoniae* and the *Enterobacteriaceae* accounted for 86 (58.5%) of the 147 isolates (Table 2). As expected, *Escherichia coli* and *Streptococcus agalactiae* accounted for more than half (29; 50.9%) of the 57 pathogens detected from infants up to 2 months old but were infrequently recovered from older children. Although *S. pneumoniae* was isolated from the blood of children of all ages, it was detected most frequently and was the predominant pathogen in patients 2 months to 1 year old. Polymicrobic bacteremia occurred in 5 (3.6%) of the 140 septic episodes, and yeasts were recovered in only 3 (2.1%) of the episodes. Anaerobes were detected in 3 (3.5%) of the 86 episodes for which anaerobic culture bottles were inoculated.

Of the 121 patients whose pathogen concentration in blood could be determined because of positive Isolator cultures, 73 (60.3%) had low-level bacteremia (≤10 CFU/ml) and 28 (23.1%) had extremely low pathogen concentrations (≤1.0 CFU/ml), including 38% of those with *Staphylococcus aureus* and over one-third of those with *Enterobacteriaceae* (Table 3). Concentrations of ≤10 CFU/ml for one or more pathogens were found in the blood of four of five children with polymicrobic bacteremia and five of seven who died. The average detection times were 23.2 h (range, 10 to 61 h) for low-level bacteremia and 17.5 h (range, 8 to 48 h) for high-level bacteremia. These differences in detection times were not significant. Detection times when only bottles were positive ranged up to 91 h.

From one 2-year-old patient, only a single colony of *Streptococcus pyogenes* was recovered from 1 ml of blood (1 CFU/ml) on one Isolator-inoculated culture plate. Two bottles and another Isolator inoculated with a total of 7 ml of blood from this child were all culture negative. From another child (1 month old), only two colonies of *S. pyogenes* (1.3 CFU/ml) were recovered from one Isolator, which contained 1.5 ml of blood, while two other culture devices (another Isolator and an anaerobic bottle) inoculated with a total of 11.5 ml of additional blood also failed to recover the pathogen.

False-negative results for Isolators or bottles were very common for our young patient population. Of 144 pathogens re-

TABLE 2. Pathogens recovered from the blood of 137 children up to 15 years old

Pathogen	No. (%) of patients with pathogens[a]	No. of patients at the following age:				
		Newborn–60 days	61 days–1 yr	1–5 yr	5–10 yr	10–15 yr
Corynebacterium spp.	2 (1.4)	1		1		
Staphylococcus spp.						
S. aureus	16 (10.9)	4	3	2	4	3
S. epidermidis	6 (4.1)	5			1	
Coagulase negative, other[b]	2 (1.4)	2				
Streptobacillus moniliformis	1 (0.7)				1	
Streptococcus spp.						
S. agalactiae	11 (7.5)	10	1			
S. pneumoniae	48 (33.6)	2	30	9	3	4
S. pyogenes	3 (2.0)	1	1	1		
Viridans group	2 (1.4)				1	1
Enterococcus spp.	4 (2.7)	2	2			
Capnocytophaga spp.	1 (0.7)	1				
Enterobacteriaceae						
Escherichia coli	27 (18.4)	19	4	3		1
Other[c]	11 (7.5)	5	3	1	2	
Flavobacterium meningosepticum	1 (0.7)	1				
Haemophilus influenzae	4 (2.7)	2	2			
Moraxella catarrhalis	1 (0.7)			1		
Neisseria meningitidis	1 (0.7)				1	
Candida spp.[d]	3 (2.0)	1	1			1
Anaerobes[e]	3 (2.0)	1		1		1
Total	147	57	47	19	13	11

[a] Five children had polymicrobic infections (two with three species each and three with two species each), and two children had multiple septic episodes.
[b] The other staphylococci (*n*) included *Staphylococcus warneri* (1) and *Staphylococcus* species with no further identification (1).
[c] The other *Enterobacteriaceae* (*n*) included *Klebsiella pneumoniae* (3); *Salmonella* species (3), including one *Salmonella* serogroup Typhi; *Enterobacter cloacae* (2); *Enterobacter aerogenes* (1); *Enterobacter agglomerans* (1); and *Serratia marcescens* (1).
[d] The *Candida* spp. (*n*) included *Candida albicans* (2) and *Candida lusitaniae* (1).
[e] The anaerobes (*n*) included *Clostridium perfringens* (2) and *Bacteroides ovatus* (1).

covered when two or more culture devices were inoculated, 85 (59.0%) failed to grow from one or more of the culture devices, which were often inoculated with as much as 5 to 10 ml of blood each. For example, of pathogens recovered when only two culture devices were inoculated, 10 (43.5%) of 23 failed to grow from one of the devices. Of pathogens detected when three blood culture devices were used, 13 (20.6%) and another 21 (33.3%) of 63 failed to be recovered from one and two of the devices, respectively. When four blood culture devices were inoculated and pathogens were recovered, three of the four devices produced false-negative results for 6 (33.3%) of 18 significant isolates. An 8-year old patient from whose blood *Streptobacillus moniliformis* was recovered (and who had previously been bitten on the lip by a rat) had six culture devices inoculated, all within 20 min. These devices consisted of two Isolators each with 1 ml of blood, two aerobic bottles each with 5 ml of blood, and two anaerobic bottles each with another 5 ml of blood. The pathogen was recovered from only one anaerobic bottle of the six devices inoculated, and the detection time was 91 h. No other sites were cultured for this patient. A 2-day-old patient from whom the *Salmonella* species was recovered had three blood culture devices inoculated, two Isolators with 1.5 ml of blood each and an anaerobic bottle with 5 ml of blood. The pathogen was recovered only from the bottle. No other sites were cultured.

From patients with pathogens in blood, the pathogens were recovered from 199 (68.2%) of 292 Isolators, 106 (75.2%) of 141 aerobic bottles, and 86 (64.7%) of 133 anaerobic bottles inoculated. Even though the bottles were often inoculated with larger blood volumes than the Isolators, there was a direct relationship between the quantitative recovery of pathogens with Isolators and the detection of the same organisms in bottles. Aerobic bottles detected 69.6% (16 of 23), 83.3% (25 of 30), and 86.1% (31 of 36) of the pathogens when 0.1 to 1.0, 1.1 to 10, and >10 CFU, respectively, of the pathogens per ml of blood were recovered with the Isolators. Similarly, anaerobic bottles detected 46.4% (13 of 28), 71.0% (22 of 31), and 89.3% (25 of 28) of the pathogens when 0.1 to 1.0, 1.1 to 10, and >10 CFU, respectively, of the pathogens per ml of blood were detected with the Isolators.

Of 135 patients from whose blood pathogens were recovered and for whom antibiotic pretreatment records were available, only 10 (7.4%) of the children (or their mothers, if infants were bacteremic within 4 days of birth) had been pretreated within 4 days of blood sample collection. Seven of the 10 pretreated children had been given antibiotics, either alone or in combination, which were later determined to be appropriate for the recovered pathogens; 5 (71.4%) of those 7 had low-level bacteremia. Of the 128 children for whom antibiotic therapy records were complete (7 patients died soon after blood sample collection), therapy was either started or changed following notification of positive blood cultures for 88 (68.8%), including 1 of 3 patients with anaerobes, 2 of 4 (for whom records were complete) with polymicrobic bacteremia, 53.7% (22 of 41) with *S. pneumoniae*, 75.0% (18 of 24) with *E. coli*, 78.6% (11 of 14) with *S. aureus*, and 90.9% (10 of 11) with *S. agalactiae*. After the notification of positive blood cultures, therapy was begun for only 5 (5.7%) of the 88 children and was changed for the remaining 83. The changes in therapy after reports of positive blood cultures resulted in more specific antibiotics with reduced spectra of activity for 76 (59.4%) of the 128 patients and a reduction in antibiotic costs for 69 (53.9%) of the patients. Changes to the use of fewer antibiotics were made for 45

TABLE 3. Relative concentrations of Isolator-recovered pathogens from septic episodes in children

Pathogen (no. of septic episodes)	No. (%) of Isolator-recovered pathogens detected at the following CFU/ml of blood[a]:			
	≤1.0	1.1–10	10.1–50	>50
Corynebacterium spp. (2)		1 (50)		1 (50)
Staphylococcus spp.				
S. aureus (13)	5 (38)	4 (31)	2 (15)	2 (15)
S. epidermidis (6)		1 (17)	1 (17)	4 (67)
Coagulase negative, other (2)				2 (100)
Streptococcus spp.				
S. agalactiae (9)	1 (11)	3 (33)	3 (33)	2 (22)
S. pneumoniae (41)	9 (22)	17 (41)	5 (12)	10 (24)
S. pyogenes (3)	1 (33)	1 (33)	1 (33)	
Viridans group (1)			1 (100)	
Enterococcus spp. (4)	1 (25)	2 (50)		1 (25)
Capnocytophaga spp. (1)		1 (100)		
Enterobacteriaceae				
Escherichia coli (22)	6 (27)	9 (41)	4 (18)	3 (14)
Other (8)	4 (50)	2 (25)	1 (13)	1 (13)
Flavobacterium meningosepticum (1)				1 (100)
Haemophilus influenzae (3)		2 (67)	1 (33)	
Moraxella catarrhalis (1)		1 (100)		
Neiseria meningitidis (1)				1 (100)
Candida spp. (3)	1 (33)	1 (33)		1 (33)
Total (121)	28 (23.1)	45 (37.2)	19 (15.7)	29 (24.0)

[a] If multiple Isolator cultures were positive for any one septic episode, the Isolator culture with the highest recovery in CFU per milliliter was recorded. A total of 121 patients had one or more Isolators with significant microbial isolates.

(35.2%) of the patients. The average total, inclusive cost per case per day at York Hospital is $1,237.00.

DISCUSSION

In our community hospital's population of children from birth to 15 years of age, low-level bacteremia was quite common, occurring in 60% of those whose culture results could be quantified using Isolators, four of five with polymicrobic bacteremia, and five of seven who died. Pathogens from 23% of the children with bacteremia were detected as only a single colony (≤1 CFU/ml of blood) from Isolators inoculated with up to 10 ml of blood. The frequency of low-level bacteremia in our pediatric population is higher than that (up to 38%) in other similar populations, as previously reviewed (20), and only a little lower than the 73% which we have found in our predominantly adult population (18). The accuracy of the determination of the frequency of low-level bacteremia in any population is heavily dependent on the routine culturing of sufficient volumes of blood.

The common recovery of pathogens at ≤10 CFU/ml from our younger patients, along with the frequent occurrence (59%) of false-negative results for blood culture devices when two or more were used for these patients, underscores the need to safely collect up to 4.5% of a patient's total blood volume in order to detect low concentrations of pathogens in the blood. A patient's total blood volume is related primarily to weight. Our laboratory has previously indicated the approximate total blood volumes of patients of various weights and ages (20). In that review, it was concluded that up to 4 or 4.5% of a patient's total blood volume could usually be used for blood cultures, allowing for additional blood volumes for other laboratory tests (up to a point) without jeopardizing the health of the patient. The current study did not address the possibility of inoculating all of the blood into a single bottle. However, the combination of Isolators (or, in other laboratories, bottles with antibiotic-inactivating material) and conventional aerobic and/or anaerobic bottles in each blood culture set allows for adequate dilution of blood and maximizes the chances of recovery of pathogens such as *S. pneumoniae* (which may not be reliably recovered from Isolators [18]), pathogens from pretreated patients or patients with low-level bacteremia from other causes, and anaerobes. Since the conclusion of the study, because so few anaerobes were recovered, blood from low-birth-weight (≤1-kg) newborns is usually inoculated into aerobic bottles (in addition to Isolators) to maximize the detection of aerobic pathogens. The routine use of multiple blood culture devices also may be of assistance in distinguishing pathogens from contaminants. The higher percentage of pediatric patients with low-level bacteremia in the current study than in previous reports may be due to the blood volumes cultured, the combination of Isolators and bottles used, or patient population differences.

The sensitivities of Isolators and bottles for microbial pathogens were not compared in the current study due to the different blood volumes frequently inoculated into the culture devices making up a set. However, neither Isolators, aerobic bottles, nor anaerobic bottles allowed for the detection of more than 75% of the pathogens when other blood culture devices used for the same patients during the same septic episodes were positive. This finding again illustrates the importance of both blood volume cultured and the routine use of two or more types of culture devices. Despite the frequently larger volumes of blood inoculated into bottles than into Isolators, the higher the concentration of pathogens in the blood (as determined with Isolators), the greater the likelihood of detection of the pathogens in the bottles. False-negative blood culture bottles were more common for patients with low-level bacteremia than for those with high concentrations of pathogens in the blood. The relative concentration of microorganisms in the blood is due to various factors, including antibiotic pretreatment, the severity of disease, and species and strain variations (3, 20, 37). While up to 48% of pediatric patients have been reported to be receiving antibiotics at the time when blood cultures are collected (3, 20, 24), only 7.4% of patients from whom pathogens were detected in the current study had been given antibiotics immediately prior to culture collection. Therefore, factors in addition to antibiotic pretreatment accounted for the majority of our cases of low-level bacteremia.

Culturing larger volumes of blood from our pediatric patients is expensive in terms of both material and labor. However, in addition to potentially improving patient outcomes, such an aggressive approach may result in substantial short- and long-term savings for hospitals, related to a reduction in the use of unnecessary empiric antibiotics once pathogens are detected (or ruled out [14]), a decrease in the duration of hospital stays, and a reduction in the emergence of antibiotic-resistant pathogens within the hospital environment. In addition, documentation of pathogens in the blood associated with another (primary) focus of infection may result in additional reimbursement to the hospital. In the current study, of the children for whom antibiotic therapy following notification of positive blood cultures could be determined, empiric therapy was changed for 64.8%, including reduced antibiotic costs for 53.9% and reduced spectra of activity for 59.4%. The cost of unnecessary antibiotic therapy has been reported to range from $158 to $716 per patient (2, 36). The average savings for York Hospital if a patient's stay can be reduced by only 1 day is $1,237. Boschman et al. have reported that there has been an average of a $3,819 (range, $2,467 to $13,497) increase in

reimbursement following the isolation of a bloodstream pathogen associated with a respiratory, gastrointestinal, cardiovascular, renal, or skin infection (4).

Low-level bacteremia is common in our pediatric patient population. Its detection has been optimized by culturing up to 4 or 4.5% of a patient's total blood volume. Potential advantages of such an approach have included increased detection of pathogens, a reduction in detection times, an improved ability to differentiate pathogens from saprophytes, assistance in the selection of specific antibiotics when a pathogen is detected, and both a reduction of hospital costs (due to appropriate antibiotic changes and reduced duration of hospital stays) and an increase in reimbursement associated with the increased detection and identification of pathogens.

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REFERENCES

1. **Albers, W. H., C. W. Tyler, and B. Boxerbaum.** 1965. Asymptomatic bacteremia in the newborn infant. J. Pediatr. **69:**193–197.
2. **Arbo, M. D. J., and D. R. Snydman.** 1994. Influence of blood culture results on an antibiotic choice in the treatment of bacteremia. Arch. Intern. Med. **154:**2641–2645.
3. **Bell, L. M., G. Alpert, J. M. Campos, and S. A. Plotkin.** 1985. Routine quantitative blood cultures in children with *Haemophilus influenzae* or *Streptococcus pneumoniae* bacteremia. Pediatrics **76:**901–904.
4. **Boschman, C. R., L. J. Tucker, D. C. Dressel, C. C. Novak, R. T. Hayden, and L. R. Peterson.** 1995. Optimizing detection of microbial sepsis. A comparison of culture systems using packaged sets with directions for blood collection. Diagn. Microbiol. Infect. Dis. **23:**1–9.
5. **Buetow, K. C., S. W. Klein, and R. B. Lane.** 1965. Septicemia in premature infants. The characteristics, treatment, and prevention of septicemia in premature infants. Am. J. Dis. Child. **110:**29–41.
6. **Byl, B., P. Clevenbergh, F. Jacobs, M. Struelens, F. Zech, A. Kentos, and J.-P. Thys.** 1999. Impact of infectious disease specialists and microbiological data on the appropriateness of antimicrobial therapy for bacteremia. Clin. Infect. Dis. **29:**60–66.
7. **Canney, R., E. B. McNamara, N. Alansari, B. Loo, and E. G. Smyth.** 1997. The impact of blood culture reporting and clinical liaison on the empiric treatment of bacteremia. J. Clin. Pathol. **50:**1010–1012.
8. **Dunne, W. Jr., J. Tillman, and P. L. Havens.** 1994. Assessing the need for anaerobic medium for the recovery of clinically significant blood culture isolates in children. Pediatr. Infect. Dis. J. **13:**203–206.
9. **Durbin, W. A., E. G. Szymczak, and D. A. Goldmann.** 1978. Quantitative blood cultures in childhood bacteremia. J. Pediatr. **92:**778–780.
10. **Eitzman, D. V., and R. T. Smith.** 1957. The significance of blood cultures in the newborn. Am. J. Dis. Child. **94:**601–603.
11. **Franciosi, R. A., and B. E. Favara.** 1972. A single blood culture for confirmation of the diagnosis of neonatal septicemia. Am. J. Clin. Pathol. **57:**215–219.
12. **Gotoff, S. P., and R. E. Behrman.** 1970. Neonatal septicemia. J. Pediatr. **76:**142–153.
13. **Hammerberg, O., H. Bialkowska-Hobranzanska, D. Gregson, H. Potters, D. Gopaul, and D. Reid.** 1992. Comparison of blood cultures with corresponding venipuncture site cultures of specimens from hospitalized premature neonates. J. Pediatr. **120:**120–124.
14. **Hurst, M. K., and B. A. Yoder.** 1995. Detection of bacteremia in young infants: is 48 hours adequate? Pediatr. Infect. Dis. J. **14:**711–712.
15. **Isaacman, D. J., R. B. Karasic, E. A. Reynolds, and S. J. Kost.** 1996. Effect of number of blood cultures and volume of blood on detection of bacteremia in children. J. Pediatr. **128:**190–195.
16. **Jacobs, R. F., M. K. Sowell, M. Moss, and D. H. Fiser.** 1990. Septic shock in children: bacterial etiologies and temporal relationships. Pediatr. Infect. Dis. J. **9:**196–200.
17. **Kaditis, A. G., A. S. O'Marcaigh, K. H. Rhodes, A. L. Weaver, and N. K. Henry.** 1996. Yield of positive blood cultures in pediatric oncology patients by a new method of blood culture collection. Pediatr. Infect. Dis. J. **15:**615–620.
18. **Kellogg, J. A., D. A. Bankert, J. P. Manzella, K. S. Parsey, S. L. Scott, and S. H. Cavanaugh.** 1994. Clinical comparison of Isolator and thiol broth with ESP aerobic and anaerobic bottles for recovery of pathogens from blood. J. Clin. Microbiol. **32:**2050–2055.
19. **Kellogg, J. A., F. L. Ferrentino, M. H. Goodstein, J. Liss, S. L. Shapiro, and D. A. Bankert.** 1997. Frequency of low-level bacteremia in infants from birth to two months of age. Pediatr. Infect. Dis. J. **16:**381–385.
20. **Kellogg, J. A., F. L. Ferrentino, J. Liss, S. L. Shapiro, and D. A. Bankert.** 1994. Justification and implementation of a policy requiring two blood cultures when one is ordered. Lab. Med. **25:**323–330.
21. **Kennaugh, J. K., W. W. Gregory, K. R. Powell, and J. O. Hendley.** 1984. The effect of dilution during culture on detection of low concentrations of bacteria in blood. Pediatr. Infect. Dis. **3:**317–318.
22. **Lee, G. M., and M. B. Harper.** 1998. Risk of bacteremia for febrile young children in the post-*Haemophilus influenzae* type b era. Arch. Pediatr. Adolesc. Med. **152:**624–628.
23. **Murray, P. R., E. J. Baron, M. A. Pfaller, F. C. Tenover, and R. H. Yolken (ed.).** 1999. Manual of clinical microbiology, 7th ed. American Society for Microbiology, Washington, D.C.
24. **Neal, P. R., M. B. Kleiman, J. K. Reynolds, S. D. Allen, J. A. Lemons, and P.-L. Yu.** 1986. Volume of blood submitted for culture from neonates. J. Clin. Microbiol. **24:**353–356.
25. **Noel, G. J., and P. J. Edelson.** 1984. *Staphylococcus epidermidis* bacteremia in neonates: further observations and the occurrence of focal infection. Pediatrics **71:**832–837.
26. **O'Grady, N. P., P. S. Barie, J. G. Bartlett, T. Bleck, G. Garvey, J. Jacobi, P. Linden, D. G. Maki, M. Nam, W. Pasculle, M. Pasquale, D. L. Tribett, and H. Masur.** 1998. Practice guidelines for evaluating new fever in critically ill patients. Clin. Infect. Dis. **26:**1042–1059.
27. **Paisley, J. W., and B. A. Lauer.** 1994. Pediatric blood cultures. Clin. Lab. Med. **14:**17–30.
28. **Reimer, L. G., M. L. Wilson, and M. P. Weinstein.** 1997. Update on detection of bacteremia and fungemia. Clin. Microbiol. Rev. **10:**444–465.
29. **Saez-Llorens, X., S. Vargas, F. Guerra, and L. Coronado.** 1995. Applications of new sepsis definitions to evaluate outcome of pediatric patients with severe systemic infections. Pediatr. Infect. Dis. J. **14:**557–561.
30. **Schelonka, R. L., M. K. Chai, B. A. Yoder, D. Hensley, R. M. Brockett, and D. P. Ascher.** 1996. Volume of blood required to detect common neonatal pathogens. J. Pediatr. **129:**275–278.
31. **Sidebottom, D. G., J. Freeman, R. Platt, M. F. Epstein, and D. A. Goldmann.** 1988. Fifteen-year experience with bloodstream isolates of coagulase-negative staphylococci in neonatal intensive care. J. Clin. Microbiol. **26:**713–718.
32. **Solorzano-Santos, F., M. Miranda-Novales, B. Leanos-Miranda, H. Diaz-Ponce, and G. Palacios-Saucedo.** 1998. A blood micro-culture system for the diagnosis of bacteremia in pediatric patients. Scand. J. Infect. Dis. **30:**481–483.
33. **Squire, E., B. Favara, and J. Todd.** 1979. Diagnosis of neonatal bacterial infection: hematologic and pathologic findings in fatal and nonfatal cases. Pediatrics **64:**60–64.
34. **St. Geme, J. W., III, L. M. Bell, S. Baumgart, D. T. D'Angio, and M. C. Harris.** 1990. Distinguishing sepsis from blood culture contamination in young infants with blood cultures growing coagulase-negative staphylococci. Pediatrics **86:**157–162.
35. **Szymczak, E. G., J. T. Barr, W. A. Durbin, and D. A. Goldmann.** 1979. Evaluation of blood culture procedures in a pediatric hospital. J. Clin. Microbiol. **9:**88–92.
36. **Trenholme, G. M., R. L. Kaplan, P. H. Karakusis, T. Stine, J. Fuhrer, W. Landau, and S. Levin.** 1989. Clinical impact of rapid identification and susceptibility testing on bacterial blood culture isolates. J. Clin. Microbiol. **27:**1342–1345.

36a. **Wassertheil-Smoller, S.** 1990. Biostatistics and epidemiology. A primer for health professionals, p. 40–41. Springer-Verlag, New York, N.Y.

37. **Welch, D. F., R. K. Scribner, and D. Hensel.** 1985. Evaluation of a lysis direct plating method for pediatric blood cultures. J. Clin. Microbiol. **21:**955–958.
38. **Winchester, D. D., J. K. Todd, and M. H. Roe.** 1977. Bacteremia in hospitalized children. Am. J. Dis. Child. **131:**753–758.
39. **Wiswell, T. E., and W. E. Hachey.** 1991. Multiple site blood cultures in the initial evaluation for neonatal sepsis during the first week of life. Pediatr. Infect. Dis. J. **10:**365–369.
40. **Yagupsky, P., and F. S. Nolte.** 1990. Quantitative aspects of septicemia. Clin. Microbiol. Rev. **3:**269–279.