Pediatric blood culture: time to positivity

Ateş Kara[1], Güler Kanra[1], A. Bülent Cengiz[1], Menekşe Apiş[1], Deniz Gür[3]

[1]Section of Infectious Diseases, Department of Pediatrics and [2]Clinical Microbiology Laboratory, Hacettepe University Faculty of Medicine, Ankara, Turkey

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The aim of this study was to determine how long it takes blood culture to become positive using a blood culture system that can be monitored continuously in pediatric patients.

Data were collected prospectively on 1,000 positive blood culture results from a tertiary pediatric university hospital from April 2000 to May 2002. The laboratory used the BACTEC 9120 fluorescent blood culture system.

Patient's age ranged from less than a day to 20 years of age (mean 3 years).

Five hundred and four cultures (50.4%) out of 1,000 yielded coagulase negative staphylococcus (CNS), 81 (8.1%) S. aureus, 53 (5.3%). Pseudomonas and 50 (5.0%) Klebsiella species. Of the 504 coagulase negative staphylococcal blood culture isolates, 314 (62.3% of CNS) were regarded as skin contaminants. Of the 1,000 cultures, 9.6% were reported as positive in the first day, 27.8% in the second day, 54.7% in the third day, 77.0% in the fourth and 89.4% in the fifth day. There was no association between previous antibiotic usage and the period required for isolate recovery.

The clinician can expect to get results of positive blood cultures with susceptibility data, at a rate of 77.1% by day four and almost 90% by day five of sampling in the bacteriemic patient. Blood cultures yielding coagulase negative staphylococci in the first three days almost always show bacteremia with those microorganisms.

Key words: blood cultures, sepsis, bacteremia, BACTEC.

Fever is a common problem in pediatric practice. In the evaluation of febrile children, physical examination alone is insufficient to identify children at risk. A wide variety of strategies for management of febrile children have been developed, almost all of which recommend having blood cultures[1-5]. Blood cultures play an integral role in the evaluation of febrile patients since rapid detection of bacteremia and fungemia is important in the management of the patient with possible sepsis[6]. In the past, laboratory identification of positive cultures by direct manual observation and plating techniques, with the earliest time for a blood culture to be positive of 36-72 hours, resulted in a delay in the follow-up of patients[7]. Since 1970, a number of automated blood culture instruments have been developed that monitor the bottles twice a day and decrease the time required to detect bacterial growth. In the 1990's manufacturers developed three different blood culture systems that can be monitored continuously[8]. These systems electronically monitor blood culture bottles 24 hours a day, typically checking each bottle every 8-10 minutes. To date, all comparative studies have shown that continuously monitored blood culture systems detect positive cultures sooner than conventional manual methods[9-14]. The present study evaluated the use of a continuously monitored BACTEC 9120 fluorescent blood culture system for children in a large tertiary pediatric hospital. This study was performed to determine the time to detection of positive cultures in pediatric patients.

Material and Methods

We prospectively evaluated all positive blood cultures in pediatric patients from 1 April 2000 to 1 May 2002 in Hacettepe University İhsan Doğramacı Children's Hospital. All pediatric

specialties and subspecialties, with both newborn and pediatric intensive care units are present at the hospital, resulting in a diverse patient population.

All positive blood cultures were obtained from patients from all patient care units at İhsan Doğramacı Children's Hospital who ranged in age from preterm newborn to 20 years, with approximately 45% of the patients being under two years of age. Using a standardized form, data concerning microorganisms identified, numbers of days from inoculation to report of positive results with susceptibility data, source of the blood culture (peripheral versus central line), patient age and antimicrobial therapy of patient at the time of sample collection were recorded.

BACTEC^{Tm}/F blood culture media that permit screening for bacteria, yeast and fungi were used throughout the study period. A single bottle was used for each blood culture ordered and a maximum 4 ml of blood was requested but not required. Both physicians and laboratory workers were blinded to the study to prevent influencing the routine practices. BACTEC 9120 fluorescent system provides continuous agitation of blood culture bottles and monitors the carbon dioxide (CO_2) content within each bottle every 10 minutes. A positive blood culture was identified when CO_2 concentration within an individual bottle rose from its predetermined baseline, and was reported as positive. Bottles were incubated for a total of 10 days before being reported as negative. Organisms isolated from each positive blood culture were identified by the pediatric microbiology laboratory section of the hospital's clinical laboratory department.

Only cultures in which a single organism was recovered were used to calculate the average time to positivity with susceptibility data.

t test for independent samples was used to compare the effect of antibiotics on timing of culture results.

Results

During the study period, 8,942 blood cultures were performed at İhsan Doğramacı Children's Hospital. One thousand blood cultures were positive (11.18%) (Fig. 1). Patient's age ranged from less than a day to 20 years of age (mean 3 years).

Five hundred and four cultures (50.4%) out of 1,000 yielded coagulase negative staphylococcus (CNS), 81 (8.1%) S. aureus, 53 (5.3%) Pseudomonas and 50 (5.0%) Klebsiella species. The list of the microorganisms identified and the range of incubation period are given in Table I.

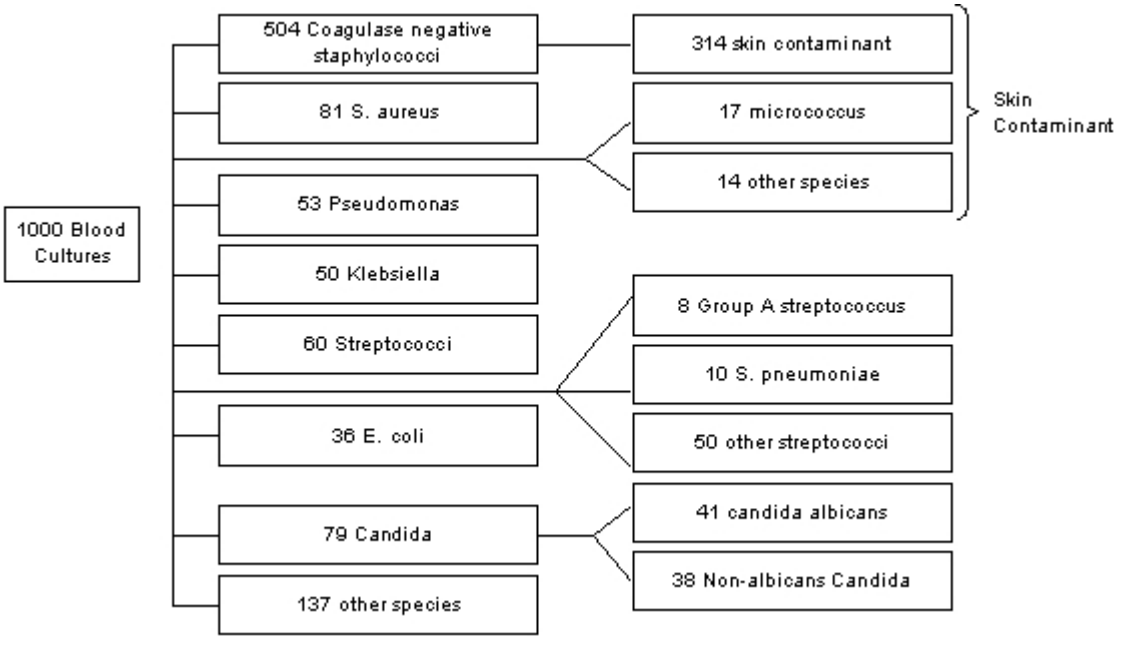

Fig. 1. Culture results.

Table I. Time to Positivity for Individual Organisms

Microorganism	Mean time (day)	N (%)
Coagulase negative staphylococcus	3.64	504 (50.4)
S. aureus	3.14	81 (8.1)
Pseudomonas spp.	2.75	53 (5.3)
Klebsiella spp.	2.88	50 (5.0)
E. coli	3.27	36 (3.6)
Enterococcus spp.	3.87	31 (3.1)
Group A streptococcus	3.12	8 (0.8)
S. pneumoniae	3.4	10 (1.0)
Other streptococcus	3.64	50 (5.0)
Acinetobacter spp.	4.33	9 (0.9)
Stenotrophomonas maltophilia	4.66	9 (0.9)
Salmonella spp.	4.5	6 (0.6)
Serratia spp.	3.1	20 (2.0)
Enterobacteriaceae	2.5	15 (1.5)
Micrococcus spp.	5.2	17 (1.7)
H. influenzae	3.0	1 (0.1)
Candida albicans	3.19	41 (4.1)
Nonalbicans Candida	3.63	38 (3.8)
Others	4.2	24 (2.4)

Of the 504 coagulase negative staphylococcal blood culture isolates 314 (62.3% of CNS) were regarded as skin contaminants. In addition, 17 micrococcus species and 14 other different types of saprophytes that colonize the skin were regarded as contaminants after clinical judgment, repeated negative blood culture results and/or clinical follow-up. As a result 345 (34.5%) out of 1,000 blood cultures consisted of skin contaminants.

Of the 1,000 cultures 9.6% were reported as positive in the first day, 27.8% in the second day, 54.7% in the third day, 77.0% in the fourth day and 89.4% in the fifth day.

Cultures yielding pathogens that were of critical importance for a specific population in pediatric patients, namely, Pseudomonas, Klebsiella, E. coli, and S. aureus as nosocomial pathogens and S. pneumoniae, Group A and B streptococcus and Salmonella species for community-acquired infections were tabulated according to growth time (Table II).

Blood cultures containing contaminants became positive at a slower rate than cultures that contained pathogens (3.12 vs 4.5 days; $p<0.001$). In the case of CNS, contaminants became positive in 4.48 days, whereas pathogens were reported as positive in 2.27

Table II. Critical Microorganisms

		Days of incubation to positivity								
Microorganism	#	1	2	3	4	5	6	7	8	9-↑
Pseudomonas	53	17	8	14	9	1	2	–	–	2
	%	32.1	15.1	26.4	17.0	1.9	3.8			3.8
Klebsiella	50	10	11	13	9	5	2	–	–	–
	%	20.0	22.0	26.0	18.0	10.0	4.0	–	–	–
E. coli	36	3	10	11	7	2	1	–	–	2
	%	8.3	27.8	30.6	19.4	5.6	2.8	–	–	5.6
S. aureus	81	5	19	27	18	9	2	1	–	–
	%	6.2	23.5	33.3	22.2	11.1	2.5	1.2	–	–
S. pneumoniae	10	1	1	5	1	1	–	1	–	–
	%	10.0	10.0	50.0	10.0	10.0	–	10.0	–	–
GAS*	8	2	1	4	–	–	–	–	–	1
	%	25.0	12.5	50	–	–	–	–	–	12.5
Salmonella	6	–	1	–	2	1	2	–	–	–
	%	–	16.7	–	33.3	16.7	33.3	–	–	–
Candida albicans	41	5	10	7	13	4	1	–	–	–
	%	12.2	24.4	17.1	31.7	9.8	2.4	–	–	–
Non-albicans Candida	38	13	4	3	2	6	4	4	–	2
	%	34.2	10.5	7.9	5.3	15.8	10.5	10.5	–	5.3

* Group A streptococcus.

days ($p<0.001$). There was no association between previous antibiotic usage and the period required for isolate recovery (Table III).

Forty-one Candida albicans and 38 non-albicans Candida were recovered in 3.19 and 3.63 days, respectively.

Klebsiella and E. coli, were detected and reported to the clinician within the first four days of sample withdrawal in more than 95% of the cases. In the case of Pseudomonas, 50% of the isolates were reported as positive in the first two days. Because of high morbidity and

Table III. Antibiotic Usage and Time of Recovery

Microorganism	Antibiotic usage	Number	Mean	Std. Deviation
CNS	No	265	3.74	1.55
	Yes	239	3.53	1.61
S. aureus	No	37	3.35	1.20
	Yes	44	3.40	1.31
Pseudomonas spp.	No	12	2.83	1.80
	Yes	41	2.73	1.87
Klebsiella spp.	No	8	3.12	1.55
	Yes	42	2.83	1.39
E. coli	No	17	3.35	1.93
	Yes	19	3.21	1.75
Enterococcus spp.	No	7	4.57	2.69
	Yes	24	3.66	1.46
Group A streptococcus	No	8	3.12	2.53
	Yes	–	–	–
S. pneumoniae	No	10	3.40	1.64
	Yes	–	–	–
Other streptococcus	No	34	3.64	1.12
	Yes	16	3.62	1.99
Acinetobacter spp.	No	6	4.0	1.41
	Yes	3	5.0	3.46
Stenotrophomonas maltophilia	No	3	5.33	0.57
	Yes	6	4.33	2.06
Salmonella spp.	No	4	5.0	1.15
	Yes	2	3.50	2.12
Candida albicans	No	9	3.11	1.61
	Yes	32	3.21	1.40
Non-albicans Candida	No	8	3.0	2.97
	Yes	30	3.80	2.44

Statistical analysis was performed by t test for independent samples.
CNS: coagulase negative staphylococcus.

Discussion

The major focus of this study was to determine the time required for a blood culture to become positive. Such information can be used for patient management decisions in conjunction with the clinical status of the patient. This study confirms results from earlier investigations in that the majority of significant positive cultures were detected in first three to four days[13,14]. Critically important, hospital-acquired microorganisms, namely, Pseudomonas, mortality of untreated Pseudomonas bacteremia in high-risk patients, almost all guidelines recommend anti-pseudomonal therapy as empiric treatment when indicated[15]. This result might be helpful while deciding about continuation or alteration of the anti-microbial therapy in such a patient.

Untreated bacteremia may result in such complications as meningitis, pneumonia, septic arthritis, osteomyelitis and purulent pericarditis[16]. The clinical identification of

bacteremia ultimately relies on the definitive identification of an organism in the blood. But cultures yielding microorganisms that are usually saphrophytes or that colonize the skin pose a clinical problem in the febrile patient. In our study, 34.5% of all positive blood cultures were regarded as contaminants, the majority of which were CNS. Blood cultures yielding CNS, in the critically ill febrile patient, is a clinical problem and diagnostic dilemma regarding whether it is a real pathogen or just a contaminant. In our study none of the pathogenic CNS isolates were detected after the fifth day of processing. Also, none of the contaminant growth was detected on the first two days of sampling. Earlier growth of CNS in blood cultures might presage it as a pathogenic organism.

Time to isolation of the pathogens from blood samples drawn while the patient was receiving antibiotics did not differ from the pre-antibiotic samples. In the literature, it has been shown that antibiotics decrease the yield of blood cultures[17]. During the study period we used the BACTEC™/F blood culture media that contains resin, which can neutralize a variety of antibiotics thus allowing growth of microorganisms that would not occur with conventional media. Although we cannot speculate about the effect of antibiotics on the bacterial growth, it was shown in our study that antimicrobial therapy does not influence the time required for bacterial growth detection in any microorganism.

On the other hand, our study had two possible limitations. No attempt was made to control the volume of blood placed in each bottle. In this study our main aim was to detect time to positivity during standard daily practice at our institution, for this reason all the blood cultures accepted and reported from the laboratory were included. A second important point that must be emphasized is the enrolment of cultures from both just-admitted and already-admitted patients. This limits the possible speculation on the microorganism profile of blood culture results.

Based on this study, the clinician can expect to get results of positive blood cultures with susceptibility data at a rate of 77.1% by day four and almost 90% by day five of sampling in the bacteremic patient. Also, blood cultures yielding coagulase negative staphylococci in the first three days almost always show bacteremia with those microorganisms. As a result, use of a continuously monitored blood culture system could be very advantageous in conjunction with clinical status to support clinicians in making patient management decisions.

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