

Effects of Volume and Periodicity on Blood Cultures

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Received 9 May 1994/Returned for modification 16 June 1994/Accepted 15 August 1994

Blood specimens collected for culture by using the high-volume resin-based BACTEC system over an 18-month period at the Seattle Veterans Administration Center were examined in this study. Of 7,783 cultures obtained, 624 were classified as true positives. Patients in this group had between 20 and 60 ml of blood drawn per culture and separated into 10-ml aliquots for incubation. Analysis of the results stratified by cultured volume and time interval between specimen collection accorded yield advantage to culture volume at the maximal amounts tested. No advantage was observed with any particular interval of collection. Increasing cultured volume from 20 to 40 ml increased yield by 19%. Increasing cultured volume from 40 to 60 ml increased yield by an additional 10%. The same effect was seen whether cultures were drawn simultaneously or serially within 24 h. These observations support other reports demonstrating increased yield with increased cultured blood volume. However, they demonstrate increases in yield at volumes much higher than previously considered. In conclusion, this study demonstrates that high-volume blood cultures drawn serially or simultaneously return the best yields.

Over the past two decades, investigation into the detection of bacteremia by blood culture has produced marked improvement in culture media, in automation of culturing techniques, and in shortening of time required to obtain definitive results. In this pursuit, several studies have been aimed at determining the volume of blood, number of serial cultures, and incubation requirements needed for optimal bacteremic detection.

Many previous studies (2, 3, 12–16) have addressed the issue of the ideal volume of cultured blood needed for optimal bacteremic detection. All have suggested a trend toward increases in yield following increases in cultured volume. However, no studies have as yet investigated culture volumes in excess of 20 ml. Two previous studies have addressed the issue of optimal number of serial cultures needed for bacteremic detection. The latest, undertaken in 1983 by Weinstein and coworkers (19), concluded that two 15-ml serial cultures taken within 48 h of each other were able to detect 99% of confirmed bacteremic episodes. A separate study undertaken in 1975 by Washington (18) concluded that three 10-ml serial cultures taken within a 24-h period were able to detect 99% of confirmed bacteremic episodes. In both studies, however, bacteremic episodes were detected by the same cultures which were then being tested, and the number of actual bacteremic episodes may have been greater than the number of confirmed episodes. Thus the implication that two or three cultures were sufficient to detect nearly all actual bacteremias might have been misleading, as it did not take into account those bacteremias undetected within these studies.

It should be emphasized that while the two preceding studies addressed the efficacy of serial cultures separated in time, neither study investigated the ideal period of separation itself. In the 1983 study, this period was defined as 48 h or less, so that a third culture taken 4 days after the first was counted in the same series. In the 1975 study, all cultures had to be obtained within a 24-h period from the first to be counted in the same series.

Some authors have suggested that increased yields obtained

by serial cultures might be simply attributable to the increase in total volume of blood cultured (11). Traditionally, serial cultures separated in time have been obtained in order to better ensure detection of bacteremias deemed to be transient. However, the effectiveness of this practice is theoretical, as no study yet has directly addressed the efficacy of serial versus simultaneous cultures.

A final point of investigation addresses the efficacy of aerobic versus anaerobic incubation. Routine inclusion of anaerobic bottles in blood cultures has been demonstrated to be inferior in overall yield to exclusive use of aerobic bottles except in select circumstances (6, 9, 10, 17).

With the previous discussion in mind, the present study addresses a number of aspects related to blood culture yield: namely, the specific effects of volume cultured in excess of 20 ml, the number of serial cultures obtained, and changes in periodicity between serial cultures.

Blood cultures obtained at the Seattle Veterans Administration Medical Center during the 18-month period from 1 January 1990 to 30 June 1991 were examined. Culture media, incubation, and testing were performed with the BACTEC system by Johnston Laboratories. BACTEC 26 and 27 series (10-ml high-volume resin-containing) culture bottles were used throughout. Bottles were tested on the BACTEC 660 infrared detection system. House officers and nurses were instructed to obtain 20 ml of blood per culture, dividing this volume equally in 10-ml aliquots into one aerobic (BACTEC 26) and one anaerobic (BACTEC 27) bottle. Volume control was achieved by means of intensive in-service education on proper culture-drawing technique and visual inspection of bottles delivered to the laboratory. Halfway through the study, house officers and nurses were instructed to obtain an additional 10 ml of blood per venipuncture for a total volume of 30 ml per culture. This extra volume was inoculated into a second aerobic bottle. Data for each bottle were tracked independently throughout the study period. Information recorded for each positive culture included time to detection and isolate identification. Contaminant cultures were determined by the method of Tenney and colleagues (16). Using the same type of evaluation, true-positive cultures obtained in 1991 were represented as either significant or transient bacteremic episodes.

This study compared differing methods of blood culture,

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TABLE 1. Culture yield by volume and periodicity

No. of bacteremic episodes tested	Initial vol cultured (ml)	No. of episodes detected	Subsequent vol cultured (ml)	No. of additional episodes detected	Interval between cultures	Yield added by extra vol cultured (%)	P	95% confidence interval (%)
184	20	148	20	35	Simultaneous	19	<0.0001	13-25
30	20	24	20	5	10 min to 2 h apart	17	0.0313	2-31
72	20	55	20	12	2 to 24 h apart	17	<0.0003	7-26
210	20	161	20	42	Anytime within 24 h	20	<0.0001	14-26
51	20	36	40	12	Anytime within 24 h	24	<0.0003	10-37
51	40	43	20	5	Anytime within 24 h	10	0.0313	1-18

changing the variables of volume and time interval between cultures. Where comparisons of two methods of culture are presented, change in yield was defined as follows: (first-method positives - second-method positives)/(all known positives), where all known positives could include additional positives not detected by either of the methods compared. For example, comparison of 20-ml versus 40-ml cultured blood volumes took into account positives undetected at 40 ml but detected at 60 ml, the last method falling outside the comparison. Statistical analysis was performed by using the nonparametric McNemar test, exact binomial probabilities, and the normal test (4).

A total of 7,783 blood cultures from 1,477 patients were obtained and examined during this study: 5,251 in 1990 and 2,532 in 1991. Of these, 859 cultures from 427 patients grew microorganisms, for an overall positive rate of 11%. Of these, 235 cultures from 196 patients were identified as contaminated and 624 cultures from 231 patients were identified as true positives, giving an overall contaminant rate of 3% and an overall true-positive rate of 8%. Coagulase-negative staphylococci accounted for 81% of contaminant cultures. Of the 178 true-positive culture results obtained in 1991, 1 result alone was attributed to transient bacteremia and the remainder were deemed significant.

As shown in Table 1, an increase from 20 to 40 ml of blood drawn simultaneously and divided equally between aerobic and anaerobic incubation significantly increased yield by 19%. A second 20-ml blood culture set obtained at any time within 24 h of the initial set significantly increased yield by 20%. Similar increases in yield were obtained regardless of whether the second set was taken immediately, within 2 h, or within 24 h of the initial set. (To confirm this point, the difference between these similar increases was found to be statistically insignificant.) Finally, adding a third 20-ml culture set within 24 h of the initial two sets significantly increased yield by 10%.

Two conclusions are evident. The first is simple confirmation of previous studies: the more blood cultured, the better the yield. The observations of this study, however, reflect cumulative culture volumes larger than previously studied or, for that matter, routinely obtained in most hospitals. Furthermore, as no plateau in yield was observed, it can be surmised that studies of further increases in culture volume may divulge still further increases in yield.

The second conclusion addresses the efficacy of serial cultures and the optimal periodicity of these cultures. Within a 24-h period, the data presented here show no significant difference in yield between multiple cultures obtained simultaneously or those obtained at intervals. Within this period, increased yields appear to be a sole function of the overall volume of blood cultured. The value of serial cultures for improving detection of transient bacteremias is also questioned by the observation that such bacteremias appear to be relatively uncommon: 0.6% in this study.

One issue which entreats future investigation is the relevance of these conclusions to the pediatric population. At what patient age or weight should the culture volumes suggested here be obtained? Several authors have suggested an inverse relationship between microbial blood concentrations and age in early childhood bacteremias (1, 5, 7). This explains how bacteremias in infants are occasionally detected with blood cultures of less than 1 ml. Nonetheless, direct studies of culture volume and yield have never been undertaken within this population.

A recent study surveying U.S. microbiology laboratories showed widespread inadequacy in obtaining optimal volumes of blood for culture, even when a volume as low as 5 ml per culture was considered sufficient (8). This follows repeated studies (2, 3, 12-16) showing that yield is largely volume dependent. The results presented in this study demonstrate that volumes of cultured blood still larger than previously studied return the best yields. They further demonstrate that during the 24-h period following an initial culture, the exact time interval between subsequent cultures is not important. Given these findings, serial timing of culture draws could be deemphasized and further education of optimum technique could be focused on the importance of obtaining adequately large amounts of blood for culture.

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