Assessing How Many Blood Cultures Are Needed for Detecting Bloodstream Infections

In their recently published work, Lee et al. (5) have estimated the cumulative sensitivity of blood cultures in detecting bloodstream infections (BSIs) in adult inpatients using automated detection systems. They considered all instances in which at least three blood cultures per patient were taken within a 24-h period. Only cases judged to represent true infection, according to medical record review, were included. Very interesting findings were shown. For example, when only two blood cultures were considered, approximately 10% of the BSIs would be missed. In addition, important differences between microorganisms were observed. Thus, in the two blood cultures taken first, a sensitivity of 97% was reached for Staphylococcus aureus bacteremia, while just 85% sensitivity was reached for Pseudomonas aeruginosa and Candida albicans.

Lee et al. (5) discussed important potential explanations for their findings. They cited an earlier study by Cockerill et al. (3), who, having found similar results, speculated that detection of low-level bacteremia by modern blood culture systems may be improved when culturing greater volumes of blood. Lee et al. mentioned that more blood cultures may also be required for patients already on antibiotic therapy. Indeed, several earlier researches have focused on increasing blood culture sensitivity by culturing greater volumes of blood (2, 6, 7, 10, 15).

Lee et al. stated that their study design may have underestimated detection sensitivity (5). Disclosure of positive results obtained for each blood culture, i.e., not cumulative detection, could help clarify this issue. Assuming that every single culture had the same probability to be positive, an even distribution would be expected. Otherwise, it would be necessary to look for factors that could explain the differences.

It must be noted, however, that this research design has potential additional biases. Considering only those patients who were asked for three or more blood cultures, instead of the whole population (i.e., excluding patients only asked for two blood cultures), this study may have focused on special subpopulations of patients. Health professionals could have asked for more blood cultures from patients with special clinical situations, such as previous antibiotic therapy and a wide spectrum of conditions known to produce low-level or intermittent bacteremia or fungemia. Furthermore, the inclusion of the whole population with suspected BSIs would allow better analysis of the impact of taking more blood cultures. Hopefully, this could also contribute to the identification of subpopulations where this approach would be truly effective, thus improving the cost-benefit ratio. Besides its sensitivity in detecting BSIs, its effect on contamination rates should also be assessed, since the latter clearly increases the laboratory workload and costs and could also cause clinical misinterpretation (1, 13, 16).

Other issues should also be considered, such as the type of bottles used and the use of dissimilar criteria to confer clinical significance according to isolated microorganisms. More strict criteria are usually demanded for some bacteria, e.g., coagulase-negative staphylococci and viridans group streptococci, unique isolates of which tend to be considered contaminants (2, 11, 16). Thus, these bacteria are likely to be recovered from more than one blood culture considered to be significant. On the other hand, in the protocol of Lee et al. (5), each blood culture consisted of 20-ml samples equally distributed among aerobic and anaerobic bottles (10 ml each). It has been observed that the recovery rates of some microorganisms, especially Pseudomonas spp. and fungi, are significantly lower in anaerobic media than in aerobic media (4, 8–12, 17). Interestingly, in the work of Lee et al. (5), both P. aeruginosa and C. albicans showed the lowest detection rates if only one or two blood cultures were considered. As previously suggested, better recovery yields could be achieved if the aerobic/anaerobic medium ratio were increased (4, 6, 8, 14).

Determining how many blood cultures are required to reach ≥99% test sensitivity is clearly of the utmost importance. Studies like those conducted by Lee et al. (5) and Cockerill et al. (3) set the basis for carrying out prospective researches specially designed to avoid all recognizable biases.

REFERENCES

Dr. Nicola raises valid points about inherent limitations to interpretation of blood culture results based on study design. Our retrospective study (2) was designed to present “real-world” results, in comparison with data previously published by Cockerill et al. (1). The design limitations of the retrospectively collected data were recognized from the outset. An ideal prospective study would include all blood cultures and all of the commercially available blood culture systems, each with their various medium formulations and combinations thereof, as well as the additional clinical data suggested by Dr. Nicola. The resources required to conduct such a study likely would be well beyond those available to clinical microbiology laboratories, including those situated in university hospitals.

The clinical microbiology laboratory has limited or no control over many pertinent factors, including patient selection, antimicrobial prescribing practices, and number and timing of blood cultures. We are in full agreement that much still needs to be learned and that prospective studies that control or account for as many relevant variables as practical are our best resources of evidence to guide future practice.

REFERENCES
