Empiric Antimicrobial Therapy for Bacteremia: Get It Right from the Start or Get a Call from Infectious Disease

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(See the article by Bouza et al. on pages 1161–9)

The difficulty in reporting microbiologic data has always been how to transfer this information to the treating physician in a timely fashion to optimize patient care. Exactly how to achieve this data transfer has always been problematic. The physician is not always informed of the preliminary microbiologic reports of blood culture data, particularly Gram stain results, even if reported to the ward or chart. Furthermore, the treating physician does not always interpret Gram stain information correctly or is often unable to relate Gram stain results to the clinical scenario [1–5]. The indication of “gram-positive cocci” in blood culture reports represents isolated information that, by itself, is unhelpful. If there are gram-positive cocci in blood cultures, the arrangement of the organisms must be stated (i.e., whether the gram-positive cocci are arranged in pairs, chains, or clusters), which helps enormously. Additional helpful information includes the times between when blood culture samples were drawn and when blood culture results were determined to be positive. How many blood culture results are positive relative to the number of blood cultures performed? These details greatly enhance the value of interpreting microbiologic data [6, 7].

The attending physician should be familiar with the differential diagnostic possibilities for organisms that present in blood cultures as gram-positive cocci in pairs (e.g., those for Streptococcus pneumoniae vs. those for Leuconostoc species). If gram-positive cocci are arranged in chains, then streptococci are the organisms to be further identified. The treating physician should be able to approximate the streptococcal group on the basis of the likely source of bacteremia. If the source is the pharynx or skin/soft tissues, group A, B, C, or G streptococci are likely, whereas if there is a gastrointestinal/genitourinary tract focus, then enterococci are most likely. Before susceptibility data are available, the physician still has the dilemma of not knowing whether the enterococci are vancomycin susceptible or vancomycin resistant. Similarly, the reporting of “gram-positive cocci in clusters” could represent coagulase-negative staphylococci (CoNS), which could be methicillin-susceptible Staphylococcus epidermidis or methicillin-resistant S. epidermidis. “Gram-positive cocci in clusters” could also represent methicillin-susceptible Staphylococcus aureus (MSSA) or methicillin-resistant S. aureus (MRSA). If CoNS are not due to skin contamination during the blood-drawing process, cases of CoNS bacteremia are usually infections associated with intravenous lines or prosthetic implant material. If “gram-positive cocci in clusters” represent MSSA or MRSA, they may be related to intravenous lines, a skin/soft-tissue source, a bone source, or an endovascular source (e.g., endocarditis) [7–10]. The clinical scenario should be of some help in narrowing possibilities on the basis of the site of infection. Until antibiotic susceptibility results are available, the treating physician can easily treat inappropriately. The reporting of antibiotic susceptibility information partially alleviates potential ambiguity. Because the appropriateness of antimicrobial therapy depends on more than the susceptibility data and final identification of the organism, input from the infectious diseases consultant can be of considerable benefit.

To be relevant, laboratory data must always relate to the clinical situation. When there is uncertainty as to the clinical significance of the blood culture isolates or to the selection of appropriate antimicrobial therapy, the interpretation and application of microbiologic data are best done by infectious diseases consultation. It has been shown that infectious diseases consultation performed early in the decision-making process can optimize clinical outcome. All too often, infectious diseases consultation occurs late in the decision-
Antibiotic selection is primarily concerned with selecting an antimicrobial with the appropriate spectrum for the usual pathogens at the site of infection. Empirical therapy for secondary bacteremia should be directed against the usual pathogens for the infected organ from which the bacteremia originates. If the empirical antibiotic selected is highly active against the usual presumed pathogens, additional coverage of other organisms offers no disadvantage. Primary bacteremia is a more difficult problem because, by definition, has no discernible focus of infection, and broad coverage is prudent.

Determination of the appropriate spectrum for empirical therapy for bacteremia, as well for as other infectious diseases, is the most common difficulty encountered by physicians in clinical practice. Empirical therapy is about getting it right from the start, to optimize outcome, minimize therapeutic failure, minimize potential resistance, and avoid serious side effects in a cost-effective manner.

De-escalating or changing to narrower-spectrum antibiotics sounds reasonable but has no basis in fact. Opting to switch to an antibiotic with a narrower spectrum after the pathogen is identified is unnecessary if the initial selection was well thought out. In cases of polymicrobial bacteremia, all of the pathogens may not, for a variety of reasons, grow on blood cultures or from clinical specimens. If the unwary clinician narrows the spectrum to cover only the organisms that have grown on culture, the treatment regimen may provide no activity against noncultured pathogens. One also presumes that narrowing the antimicrobial spectrum also decreases the potential for resistance, but this has not shown to be the case. If the antibiotic selected for initial empirical therapy has an appropriate spectrum and a low resistance potential, there is no advantage in narrowing the spectrum. Antibiotic resistance is, in the main, agent specific, and switching to a narrower agent, per se, does not decrease resistance [19–21]. For all of these reasons, carefully selected initial empirical therapy gives the patient the best chance of a favorable clinical outcome with low resistance potential, has the fewest potential side effects, and is cost-effective for the institution.

In this issue of Clinical Infectious Diseases, Bouza and his colleagues [15] in Madrid present a unique and landmark study. Their study describes the impact of different methods of reporting positive blood culture results for patients with bacteremia to the physicians in charge. The findings are based on 297 episodes of bacteremia randomized into 3 study groups, which differed in the method of reporting positive blood culture results. Conventional microbiological results were reported in the usual fashion for the first group (group A); in the second group (group B), clinicians responsible for the patient also received a written report; and in the third group (group C), clinicians received the above, as well as an oral report. This study describes the appropriateness of empirical antimicrobial therapy, as related by method of microbiologic data reporting, on the impact and quality of clinical care from the onset of infection to discharge or death. The study was well designed and executed, eliminating microorganisms of doubtful significance and including only clinically relevant episodes for which there were clinical manifestations of infection without other explanation, and the study included only organisms isolated from ≥2 blood cultures.

The large teaching/referral hospital in Madrid, Spain, where the study was conducted, provided not only a written report after definitive isolate identification and antimicrobial susceptibilities were determined; but in the conventional reporting group (group A), physicians were telephoned the equally important results of the Gram stain of antimicrobial growth in broth culture. Other physicians (group B) in the study received a written bedside report that was included with the chart, which included specific therapeutic recommendations based on the patient’s clinical situation, as well as microbiologic information, which is more than most hospitals provide. The remaining physicians (group C) received the same information provided to the 2 previous groups at the same time, but in addition, the physician in charge was provided with a telephone consultation from an infectious diseases clinician or a clinical microbiologist.

Bouza et al. [15] are to be complimented for developing and implementing an effective, timely, and tiered method of reporting microbiologic results to the pa-
tient’s physician. In Europe, the specialty of infectious diseases is not yet fully developed, and clinical microbiologists perform many of the tasks provided by infectious diseases consultants. This landmark study demonstrates that there is a whole order of magnitude of difference between a simple laboratory report on the chart and one that is augmented in real time by a call from an infectious diseases consultant or a clinical microbiologist, providing an assessment of the significance of the blood culture isolate based on the clinical scenario. The call from the infectious diseases consultant to the attending physician represents a quantum leap in application of microbiologic information to clinical care.

The approach used by Bouza et al. [15] represents a paradigm shift in the clinical decision-making process, linking the reporting of blood culture results to the treating physician via the infectious diseases consultant. By positioning the infectious diseases consultant early in the information-transmitting sequence, the infectious diseases consultant can take into account the patient’s host defense status, age, renal or hepatic function, antibiotic allergy history, tissue penetration and pharmacokinetic considerations, and potential side effects and can be maximally effective at the most critical point in therapeutic decision making [20, 21].

In the study [15], no special interventions were applied to the conventional reporting group. Recommended changes in therapy were made in 52.3% of cases in the written report group and in 53.1% of cases in the oral report group. Recommended changes were implemented in 80% of cases in the written report group and in 95.3% of cases in the oral report group. The adequacy of antimicrobial coverage was significantly different among the 3 groups. In the late period of the study, appropriate antimicrobial selection (based on spectrum) was received in 71.1% of cases in the conventional group and in 92.1% and 91.3% of cases in the written and oral groups, respectively. Importantly, the proportion of days on which patients received antimicrobial therapy with an adequate spectrum in the late period was 66.3% for the conventional group and 92.1% and 91.2% for the written and oral report groups, respectively.

An unexpected finding of great importance was that inappropriate antimicrobial therapy was associated with increased antimicrobial cost. Inappropriate empirical antibiotic therapy was the most expensive in group A (€138 per bacteremic episode, compared with €39.8 and €35.9 per bacteremic episode in the written-report group [group B] and oral-report group [group C], respectively).

The study by Bouza et al. [15] is the first to study the impact that the method of microbiological reporting has on the appropriateness of initial therapy for bacteremia, and this is of fundamental importance. The results demonstrated that improving the delivery of microbiologic information (with the information conveyed by an infectious diseases consultant to the treating physician) made an important impact on the length of hospital stay, the infection-related and overall mortality rates, and the cost of therapy per bacteremic episode all decreased.

The study by Bouza et al. [15] clearly shows that the method of reporting microbiologic data for cases of bacteremia has an important impact on infection-related and overall mortality rates, as well as an interesting impact on length of hospital stay and the cost per bacteremic episode. The significance of such pharmacoeconomic advantages cannot be underestimated in managed health care. The cost of supporting a reporting system involving infectious diseases consultants and clinical microbiologists can be justified by the savings generated from decreased length of hospital stay and decreased costs of antimicrobial therapy. Bouza and his colleagues have shown how to maximize the usefulness of microbiologic data by having the infectious diseases clinician provide the treating physician with results and interpretive and evaluative advice before consultation is requested.

Hospitals would do well to implement such a system, not only for improved patient care but for economic reasons as well. Until such a scheme can be implemented in hospitals, we need to make improvements in selecting an appropriate therapy for bacteremia at the initiation of empirical therapy. With appropriate empirical therapy for bacteremia, the lesson is to get it right from the start so that recommendations for subsequent corrective changes in therapy become unnecessary or to get a call from the infectious disease consultant.

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