Selecting Bacteremia as the Most Appropriate Clinical Syndrome to Study

Some might argue that duration of antibiotic treatment should be driven by the underlying infectious focus, rather than the presence or absence of bacteremia. However, clinical experience suggests that the presence of bacteremia is frequently cited by physicians as a reason to extend therapy to 14 days, regardless of the underlying source. This notion is supported by the results of our national practice survey. The distributions of treatment duration recommendations were virtually identical for scenarios of bacteremic pneumonia, bacteremic pyelonephritis, catheter-related bloodstream infection, bacteremic intra-abdominal infection, and bacteremic skin and soft tissue infection, highlighting that bacteremia is a very influential syndromic aspect and the appropriate focus for our research program. Others might argue that the outcomes of these bacteremic infections are heterogeneous, and so it is not appropriate to lump these groups of patients together in one trial. However, mortality rates are in fact very similar for the bacteremic subgroup of critically ill patients with these infections, and even if they differ our trial will ultimately examine subgroups by infectious focus.

The advantages of studying bacteremia as a clinical entity versus other associated syndromes outweigh other potential disadvantages. In contrast to syndromic diagnoses (ventilator-associated pneumonia for example), all patients with bacteremia have a positive sterile site culture result (by definition). Therefore, all bacteremic patients (with non-contaminant species) have true infection, whereas the presence (or absence) of pneumonia is much harder to define because cultures may represent colonization rather than infection, and even multiple adjudications of case definitions provide only moderate agreement (particularly in patients on mechanical ventilators). Given that bacteremia is defined by the positive blood culture result, all study patients will have an identified pathogen, in contrast to syndromic infections which are often treated empirically (without a defined etiology). A corollary is that antibiotic susceptibility test results are available for all bacteremic patients, so it will be clear whether or not patients randomized to shorter versus longer duration antibiotic treatment are receiving an effective antibiotic. The bacteremic subgroups of patients with pneumonia, pyelonephritis, intra-abdominal infection, and soft tissue infection, generally have more severe and complicated courses than non-bacteremic infections. Therefore, if shorter course therapy is demonstrated to be effective for bacteremic patients, the results can be more easily generalized to non-bacteremic patients than vice versa. Finally, pre-specified subgroup analyses will examine the impact of treatment duration within each specific syndrome (e.g. pneumonia, catheter-related bloodstream infection, etc.).