suggesting that CT cannot reliably be used to predict who will or will not experience herniation after lumbar puncture. We agree with his thoughts that fear of litigation and the presumption that CT before lumbar puncture has become the standard of care are reasons that physicians persist in performing a neuroimaging study before lumbar puncture for many patients, and we agree that there is a need for a definitive prospective study to answer this important question. However, we believe that the devastating nature of brain herniation warrants caution. Our criteria (i.e., immunocompromised state, history of CNS disease, new-onset seizure, papilledema, abnormal level of consciousness, and focal neurologic deficit) for performance of CT before lumbar puncture in adult patients can be used as a guide for physicians in performing lumbar punctures in patients without any of the criteria [2], because they are less likely to have increased intracranial pressure that may lead to herniation after lumbar puncture [3]. These were essentially the criteria published by Hasbun et al. [4], who recommended that patients with these baseline clinical features and suspected meningitis should first undergo CT of the head, after emergent blood cultures have been performed and appropriate empirical antimicrobial therapy has been initiated. Although we recognize that there are some patients with intracranial mass lesions who safely undergo lumbar puncture, performance of a neuroimaging study for those patients with any of our identified criteria may also obviate the need for lumbar puncture, as other etiologies (e.g., papilledema, abnormal level of consciousness, and focal neurologic deficit) may be identified.

Kalil [5] makes the point that adjunctive dexamethasone therapy should be initiated before or with the first dose of antimicrobial therapy for all patients with suspected or proven bacterial meningitis, regardless of the microbial etiology. Dr. Kalil may be correct, but at present, we feel that the available data do not support his conclusion. We agree that, although the clinical trial by de Gans and van de Beek [6] was not adequately powered to analyze all subgroups of patients on the basis of microbial etiology, no previously published study, whether of infants and children or adults [7]—including a meta-analysis of randomized clinical trials from 1988–1996 [8]—has demonstrated a benefit for adjunctive dexamethasone therapy for patients with acute meningitis caused by bacteria other than Streptococcus pneumoniae and Haemophilus influenzae type b. Although recent trials have demonstrated that steroids are beneficial in patients with septic shock, independent of microbial etiology [9, 10], it is important to note that the benefits were only seen in patients who received physiologic doses and longer courses of corticosteroid therapy, not the high doses and short courses used in clinical studies of patients with bacterial meningitis. That said, we stated in the practice guideline that some authorities would initiate adjunctive dexamethasone therapy for all adults with suspected or proven meningitis, because the etiology is not always ascertained at the time of initial evaluation [2]; we did not give this recommendation as strong a rating, given the absence of published data for the use of adjunctive dexamethasone in adults with meningitis caused by bacteria other than S. pneumoniae.

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References


Candidemia in Patients with Cancer: Are Persistent Neutropenia and Severity of Illness Score Still Relevant?

We are pleased that Raad et al. [1] confirm our findings [2] that central venous catheters (CVC) should not always be removed from patients with candidemia, because removal would not have been beneficial in 73% of their patients. This is a welcome change from the authors’ previous recommendations [3] and from the published guidelines of the Infectious Dis-
es the Society of America [4, 5], and it supports our conclusion [2] that host variables are the most important prognostic factors for outcome. We are surprised, however, that the authors did not analyze the severity of illness and the persistence of neutropenia. Data regarding these variables were collected and reported in 7 articles that describe subgroups of the same study population [6–12]; these variables are considered critical by most investigators [2] and have been prespecified by Raad and colleagues [6–12] as potentially important. In addition, Raad and colleagues have asserted, in previous articles about subgroups of this study population, that “persistent neutropenia was a predictor of poor prognosis” [6, p. 2661], that “neutrophil counts were strongly associated with response” [7, p. 382], that “persistent neutropenia is a strong prognostic factor for poor response” [9, p. 1679], and that “not surprisingly, persistent neutropenia was a strong prognostic factor for poor response” [11, p. 1864], and had concluded that “an APACHE II score ≥16, was associated with poor outcome” [7, p. 383].

The importance of including these 2 confounding variables—the severity of illness and the persistence of neutropenia—is exemplified by our study of candidemia in a comparable population [2]. In that study, a powerful effect of CVC removal was present in findings from univariate analysis (P < .001) but not in findings of multivariate analysis (full CVC exchange, P = .061); the latter identified severity of illness, persistence of neutropenia, and dissemination as the strongest predictors of outcome (P < .001) [2]. The loss of the powerful effect of CVC removal is best explained by the significantly higher severity of illness score and rate of persistent neutropenia among patients with CVC retention versus those who underwent CVC removal (P < .001), suggesting that CVC removal is more commonly performed on patients without unfavorable prognostic factors [2].

The omission in the current manuscript [1] of the severity of illness and the persistence of neutropenia, 2 confounding variables that Raad et al. prespecified as potentially important [6–12], is troublesome. Furthermore, the main outcome predictor in their study was the response to treatment, which they defined as the resolution of clinical manifestations of candidemia with sterilization of blood cultures [1]. Because of the retrospective design of their study, blood culture (the primary end point) was not performed in a standardized fashion and “there was insufficient information to determine the role of catheters in many infections,” as has been acknowledged by the investigators of a subgroup analysis of the same population [7, p. 384]. Addressing these serious limitations could perhaps be attempted by adjusting for the number of blood cultures performed (i.e., mean, median, and range) and by describing the methodology used to account for the “many patients” for whom “there was insufficient information to determine the role of catheters” [7, p. 384]. We strongly recommend that Raad and colleagues include the confounding variables that they had prespecified as potentially important (i.e., APACHE II scores, the persistence of neutropenia, and the number of blood cultures) [6–12]. A revised analysis would be of great interest to the medical community, and, along with our recent findings [2], it would invite a revision of the guidelines of the Infectious Diseases Society of America for the management of candidemia.

Acknowledgments


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References

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Reply to Nucci and Anaissie

Sir—We disagree with the position of Nucci and Anaissie [1] and believe they have misinterpreted our study [2], the guidelines of the Infectious Diseases Society of America (IDSA) [3], and the med-