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Reply to Collins et al and Manian

To the Editor—We thank Collins et al for their data regarding the incidence of catheter-related candidemia in their patients receiving total parenteral nutrition through short-term, non-tunneled, non-antimicrobial-coated central venous catheters [1]. All such infections at their institution were due to *Candida albicans*. As noted, Chow et al [2] found that duration of total parenteral nutrition is independently associated with a decreased risk of candidemia due to non-*albicans Candida* species, compared with *C. albicans*. Chow et al [3] also found that total parenteral nutrition duration was an independent risk factor for non-*albicans* candidemia, compared with controls without candidemia. Thus, prolonged total parenteral nutrition administration increases risk of candidemia, especially, but not solely, due to *C. albicans*.

Guidelines are a framework to clinical decision making. We agree with Collins and colleagues that the interpretation of our guidelines [4] should be done in the context of local epidemiology, and we are happy that our guidelines are not in conflict with this truism.

We thank Dr Manian for his reflections on the "2 sets (1 peripheral)" recommendation of our updated Infectious Diseases Society of America guideline [4]. The primary reason to continue to recommend this policy is that, in theory, this may allow for the calculation of the differential time to positivity (DTP). In addition, in some patients, obtaining 2 peripheral blood cultures may be difficult. In our opinion, most, if not all, modern microbiology laboratories use a blood culture system with continuous monitoring for positivity and should, therefore, be able to report on the DTP. However, it is true that the use and interpretation of the DTP is only possible when both the clinician and laboratory handle blood cultures correctly, and we agree that this is not always simple. The peripheral and catheter-drawn blood cultures need to be obtained within a few minutes of each other, before antibiotic therapy is initiated, and the blood culture vehicles (eg, bottles) should be inoculated with the same volume of blood. The blood culture bottles should be properly labeled regarding the site where the blood cultures were obtained and the time the blood cultures were taken should be accurately noted. When these cultures arrive in the laboratory they both need to be placed in the incubator at the same time and the time to positivity has to be reported back to the clinician together with the time the blood culture was taken. This latter detail is important in the event that other blood cultures are taken on the same day, so that the DTP can be calculated based on blood cultures that were sampled within a few minutes of each other.

The DTP cannot always be calculated in hospitals with up-to-date microbiology equipment. Dr Manian correctly highlights the practical problems that can occur when paired blood cultures are obtained. The DTP can only be calculated when both blood cultures reveal growth. In a study on DTP in intensive care unit patients, the positive predictive value for true catheter-related bloodstream infection was poor when only the blood culture taken through the catheter demonstrated growth [5]. Unfortunately, this occurs frequently. In 1 DTP study, at least 1 of 1010 paired blood cultures revealed growth, but most often ($n = 603$), only the blood culture drawn through the catheter was positive [6]. We agree with Dr Manian that an isolated positive catheter-drawn blood culture on its own is not proof of catheter-related bloodstream infection and does not necessarily connote the need for catheter removal. However, the opposite situation (positive peripheral blood culture with a negative catheter-drawn culture) makes it very unlikely that the catheter is the source of a bloodstream infection [7]. As such, this may be an additional reason to recommend the "2 sets (1 peripheral)" policy even if the laboratory is unwilling or unable to report the DTP. In a recent review, other authors also suggest that "based on the available evidence, at least 1 blood culture should be obtained from the intravascular catheter" [8, p 1].

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Early Experience with High-Dosage Daptomycin for Prosthetic Infections

To the Editor—In the 15 July issue, Figueroa et al [1] reported the results of a retrospective medical record review for 61 patients treated with high doses of daptomycin (mean, 8 mg/kg) for a median of 25 days (range, 14–82 days) for a variety of clinical indications and concluded that treatment was well tolerated. We report here our early experience with 2 patients with orthopedic prosthetic infections who were treated with intravenous daptomycin at a dosage of 8 mg/kg/day and did not experience increased creatine phosphokinase (CPK) levels.

The first patient was a 72-year-old man who had had rheumatoid arthritis for 10 years. In February 2008, a knee prosthesis was implanted; after 12 months, he developed pain, tenderness, and stiffness of the prosthetic knee, with an increased erythrocyte sedimentation rate (ESR) (108 mm/h) and C-reactive protein (CRP) level (3.9 g/L; normal value, <0.5 g/L). At the time of admission, he had been treated for 10 days with minocycline and had a positive white blood cell scan result indicating active infection of the implanted knee prosthesis. Treatment was started on 9 June 2008 with intravenous daptomycin at 8 mg/kg/day (640 mg) and intravenous ceftriaxon at 2 g/day, and a reduction in the ESR and a quick normalization of the CRP level occurred after 3 weeks of treatment. Such treatment was continued until 29 July, when daptomycin was switched to intravenous teicoplanin at 600 mg/day because of the patient's need to move to another city for the summer holidays. During treatment with teicoplanin and ceftriaxon from 30 July to 20 August, the CRP level increased to 5.1 g/L. Daptomycin was readministered instead of teicoplanin and ceftriaxon beginning on 21 August, and the CRP level normalized after another 3 weeks of treatment. Treatment was discontinued at the end of September, and a white blood cell bone scan result was negative 6 weeks after the end of treatment. The CPK level did not increase during treatment.

The second patient was a 54-year-old man with an infection of the right tibia who had fistulization and isolation of methicillin-sensitive *Staphylococcus aureus* from the site at which multiple fractures had been treated with internal osteosynthesis 2 months earlier. The ESR and CRP level normalized after 4 weeks of treatment with intravenous daptomycin at 8 mg/kg/day, and an increased CPK level was not observed during treatment, which was very well tolerated (as in the first patient). Unfortunately, treatment was not successful in eliminating the infection, which relapsed at the end of the eighth week of treatment. Definitive treatment via surgical removal of the internal osteosynthesis was needed to achieve clinical cure.

Our results are consistent with the findings of Figueroa et al [1] and support the safety of high dosages of daptomycin for prolonged periods in the treatment of orthopedic infections. Daptomycin was administered in our outpatient clinic, where patients have free access and receive medical follow-up. We believe it will be demonstrated that daptomycin is a useful treatment for orthopedic infections, for which in vitro penetration into biofilm [2, 3] is extremely important for success. We strongly agree with Figueroa et al in recommending further studies of high dosages of daptomycin in larger cohorts.

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