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LETTER TO THE EDITOR

Author's reply

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To the Editor,

Grupper et al. [1] correctly point out that the rules and physics of pharmacokinetics/pharmacodynamics (PK/PD) apply equally well to spiked blood culture studies as they do to in vivo determinations of the free and bound concentrations of antimicrobial agents in blood. If the purpose of our study was to determine the concentrations of the study drugs in those compartments, we would have had to consider the protein bound versus free drug concentrations in our model to see if we had actually exceeded the minimum inhibitory concentration (MIC) of the test organisms in terms of the latter. However, as the authors surely noted, the first part of our study dealt only with the detection of free drug in blood culture bottles without blood in order to get an indication of the amount of each antimicrobial agent bound by the polymeric resins of either manufacturers' bottles. In the second half of the study, we were only interested in the overall recovery of organisms from either bottle type using spiked blood culture bottles containing organism [7–30 colony-forming units (CFU)/bottle: very low], 10 mL of healthy human blood, and concentrations of select antimicrobial agents intended to mimic peak serum concentrations. In other words, the model pretended that blood cultures were being drawn immediately after a standard infusion of each antibiotic. How much drug was actually free? We really didn't care because it was a sufficient concentration to exceed the MIC of the test organisms by a long shot, and it was a side-by-side comparison of bottle types. As such, we were able to relate the recovery of microorganisms from spiked blood cultures and relate those findings to the kinetics of antimicrobial binding demonstrated by the initial evaluation in the absence of bugs and blood. Yes, indeed, PK/PD occurs in spiked blood culture bottles, but there is also a complex equilibrium determined by the binding kinetics of drug to blood proteins, drug to microorganisms, and drug to polymeric resins. We re also certain that there is binding of blood protein to resins and to microorganisms. These dynamics add a level of complexity to the PK/PD of a drug in a spiked blood culture that extends far beyond the information we were looking for. In the end, we found that the rate and magnitude of polymeric resin binding of antimicrobial agents, along with a known MIC of a test organism, does a fair job of predicting recovery without knowledge of the drug's PK/PD properties, especially when the dose is extremely high.

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References

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