Bactericidal/Permeability Increasing Factors

To the Editor:

I am concerned about the bactericidal/permeability increasing (BPI) factor concentrations reported by Pereira et al. (J Am Soc Nephrol 1996;7:479–487). It is known that BPI is normally not a constituent protein of plasma. It is primarily found in the azurophil granules of granulocytes and, even after activation of the granulocyte by endotoxin, 95% remains cell-associated. In addition, it has been shown that variations in the time (minutes) between blood-taking and separation of the plasma can affect the plasma concentration by up to sevenfold (1). Given this background, it is difficult to accept the enormous scatter of BPI plasma levels reported in the article by Pereira et al. without wondering if some artefact has not crept in. The most likely cause for error is contamination of the plasma by granulocytes. Double-spinning of the plasma is the best way to avoid this artefact. This appears not to have been done in this study. Therefore, the results and conclusions of the authors that are based on BPI plasma levels should be viewed with caution.

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Response:

Thank you for giving us the opportunity to respond. The suggestions by Dr. Shaldon that the BPI levels reported in our study may have been affected by delay in plasma separation and neutrophil contamination are both invalid. The Methods section of our manuscript clearly states that blood was collected in sterile, standard vacuum blood-collection tubes containing EDTA (1.5 mg/mL of blood), and centrifuges were available in the dialysis clinic or laboratory to ensure that the tubes were immediately centrifuged (400 g, 10 min). Furthermore, plasma was removed without disturbing the buffy coat, and aliquots of 500 μL were spun at 10,000 g for 1 min at 4°C and stored at −70°C. Hence, the criticism that a delay in plasma separation or neutrophil contamination may have occurred is without basis. Moreover, under identical laboratory conditions, we observed a 6681 ± 1788% increase in plasma BPI levels at 15 min after initiating dialysis with cellulose dialyzers, unequivocally demonstrating BPI release during hemodialysis. Indeed, an identical observation has been reported by Dr. Shaldon and colleagues (1). Finally, the principal aim of our study was to study the role of LBP and BPI as modulators of endotoxin-stimulated cytokine production among patients with chronic renal failure. We have clearly demonstrated that plasma LBP:BPI ratio could influence cytokine production in response to bacterial endotoxin and that natural or pharmacological increases in plasma BPI levels and the consequent decrease in LBP:BPI ratios could attenuate this susceptibility to endotoxin-stimulated cytokine production.

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