In the present issue of *Critical Care*, Linder and colleagues present a new study in which they assess the clinical importance of serial measurements of heparin-binding protein (HBP) plasma levels in critically ill septic and nonseptic patients [1]. They found that HBP plasma levels are significantly higher in patients with severe sepsis and septic shock in comparison with patients with a nonseptic critical condition. The authors also demonstrated that HBP plasma levels obtained at admission to the ICU and during the last individual sampling are higher in nonsurvivors as compared with survivors in both the septic group and the whole study group. Moreover, the high baseline HBP plasma levels in septic patients were associated with an increased 28-day mortality rate. Altogether, these results indicate that serial HBP measurements might be very helpful in stratification of ICU patients. However, there are some issues that should be raised before the study results can be translated into the daily routine.

The study was designed to compare HBP plasma levels in patients with severe sepsis and septic shock with levels in patients with noninfectious critical illness. However, these two groups of patients were not equal in size. Also, a significant proportion of nonseptic critically ill patients developed infection while hospitalized in the ICU, and to classify them as truly nonseptic patients is problematic. Second, there is a lack of a routine diagnostic method for HBP analysis. Nevertheless, if the results of the present study are validated in large clinical trials in different ICU populations and cost-effectiveness data become available, the serial HBP measurements will have a promising future.
Other routinely measured biomarkers – such as procalcitonin, C-reactive protein, neutrophil and lymphocyte counts – have only a limited value in prognostic scoring of the critically ill patients and are mostly used in the early diagnostics of bacterial etiology of critical illness [6-8].

It is worth noting that HBP mediates multiple actions during the infectious process. Notably, HBP has antibacterial activity, which includes a direct microbicidal effect, and also helps neutrophils to migrate into the focus of infection. Similarly to HBP, C-reactive protein and IL-6 play an active role during the immune responses against infections: C-reactive protein is an inflammation opsonin, and the major function of IL-6 is amplification as well as downregulation of inflammatory reactions, depending on the concentrations [9,10]. Regarding procalcitonin, there are only limited data from animal studies – which demonstrate that immunoneutralization of procalcitonin improved survival in experimental porcine sepsis [11].

Additionally, elevated cortisol levels in peripheral blood during sepsis are considered an integral part of compensatory anti-inflammatory response syndrome, leading to downregulation of exaggerated systemic immune responses [12]. From the functional point of view, in comparison with the abovementioned biomarkers, HBP therefore plays the most complex role in severe sepsis and septic shock – highlighting its potential for clinical use.

In conclusion, the serial measurements of HBP plasma levels can be a useful tool for close monitoring of critically ill septic patients. The results of Linder and colleagues therefore warrant evaluation in different ICU populations. However, availability of a routine diagnostic method for HBP analysis is essential to confirm these interesting data.

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Abbreviations
HBP, heparin-binding protein; IL, interleukin.

Competing interests
The authors declare that they have no competing interests.