(SOFA) score and was associated with less renal replacement therapy. Building on animal and preclinical human data, the Schortgen et al[5] trial supports the safety of cooling febrile patients with septic shock and suggests that survival advantage may persist pending further study.

As clinicians, we are continually called upon to make clinical decisions absent abundant data. In this case, the best available data support external cooling in febrile patients with septic shock. No such benefit can be postulated for antipyretic drugs, and their use among critically ill patients with life-threatening infection should be discouraged. Extrapolating data from dissimilar patients and interventions is insufficient to overcome the demonstrated safety and potential benefit of external cooling in the most severely ill patients. For an intervention that has been shown to have the potential to improve mortality and absolutely no convincing evidence to suggest harm, we cannot continue to ignore mounting clinical evidence that cooling our sickest patients with septic shock may save lives.

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Rebuttal From Drs Drewry and Hotchkiss

We commend Drs Mohr and Doerschug[1] on their well-constructed argument in favor of antipyretic therapy for patients with septic shock. However, based on current evidence, we adamantly maintain that fever should not routinely be treated in all patients with septic shock. Although both our groups seem to agree that pharmacologic antipyretic therapy is unlikely to benefit these patients, we differ in our interpretation of the clinical evidence regarding external cooling. Only one large clinical trial specifically designed to investigate the benefit of external cooling in patients with septic shock exists. Schortgen et al[2] randomized 200 febrile patients with severe septic shock to 48 h of external cooling or to no fever control. The number of patients with at least a 50% vasopressor dose reduction at 12 h was greater in the group that received external cooling. Although there was a nonsignificant trend toward decreased ICU mortality in the external cooling group, there was no difference in mortality at hospital discharge. Based on these results, Drs Mohr and Doerschug conclude that "febrile patients with septic shock should be cooled using external cooling to normothermia to optimize clinical outcome."[1] We respectfully disagree.

The ability of external cooling to decrease vasopressor requirements in this study is not surprising. Previous physiologic studies in humans have consistently shown cooling to be associated with higher serum levels of norepinephrine and epinephrine, greater cutaneous vasoconstriction, and increased BP.[3,4] Unfortunately, reductions in vasopressor requirements do not directly translate to improved long-term clinical outcomes, and the hemodynamic benefits of cooling must be weighed against the potential adverse effects. External cooling induces shivering, which leads to significant increases in oxygen consumption and sympathetic activation, thereby eliminating the metabolic benefit derived from fever control.[3,5] Schortgen et al[2] reported low rates of shivering in their study; however, a large percentage of their patients received neuromuscular blockers, which may have mitigated this complication. Furthermore, antipyretic therapy prevents fever-related augmentation of the immune system and impairs the clinical recognition of new infections. This may partially explain the trend toward increased nosocomial

infections by day 14 seen in the cooled patients in Schortgen et al's[2] study.

Drs Mohr and Doerschug argue that the patients most likely to potentially benefit from fever control are those with the most severe shock. Based on their degree of organ dysfunction and baseline vasopressor doses, the patients in Schortgen et al's[2] study certainly met the description of severe shock. Despite this, no long-term mortality benefit of cooling was found. Also, the results of this study—in terms of reduced vasopressor doses and a trend toward decreased ICU mortality seen in the cooled group—should not be generalized to all patients with septic shock. Those with less severe shock may experience more harm than benefits from fever control. It seems premature to conclude that patients with septic shock should routinely be cooled based upon the results of this single study, especially considering that antipyresis has not been found to be beneficial in other studies of septic critically ill patients.[6,7]

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