the optimal timing of hypothermia relative to the onset of sepsis and related organ failures. In this regard, and in keeping with the well-stated concerns of Dr. Cunha relating to suppression of immune cell function during hypothermia, it may be best to delay the onset of hypothermia until the effects of antibiotics and the initial immune response in terms of microbial killing have been realized. Given that the current approach to managing sepsis-related organ failures is to provide "supportive care," the findings of Beurskens et al (4) are important, in that they provide hope for the emergence of hypothermia as a cytoprotective strategy to prevent potentially lethal organ failures.

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Current randomized clinical trials of red cell storage duration and patient outcomes

To the Editor:

We read with interest the report by Hu et al (1) finding that anemic rats transfused with longer stored red blood cells suffered worse damage from experimentally induced myocardial infarction than anemic rats transfused with red blood cells stored for <4 hrs. This study provides interesting evidence that outcomes were better in rats transfused with red blood cells stored for the shorter time period. Similar observations have been made in other animal model systems, but extrapolating these results to the clinic should be done with circumspection. As pointed out by the accompanying commentary, erythrocyte functioning is complex and rat and human red blood cells have substantially different rheology and storage lesions (2). Indeed, both the report by Hu et al (1) and the commentary suggest that future clinical studies are needed on this topic.

We bring to the attention of your readers the fact that several large clinical trials studying the effects of storage time on clinical outcomes are currently underway. One trial that has completed enrollment included neonatal intensive care patients (3) and two other large multicenter trials are currently enrolling patients (4, 5). One of these trials includes patients in intensive care units in Canada, while the Red Cell Storage Study is enrolling patients undergoing cardiac surgery.

We are running the National Institutes of Health-funded Red Cell Storage Study trial that includes patients who are at least 12 yrs old and undergoing cardiac surgery with risk factors predicting high likelihood of requiring red blood cell transfusion. Patients are randomized to receive either red blood cells stored no less than 10 days or red blood cells stored for at least 21 days when the latter would have been provided as part of standard care. This trial, which is still adding sites, should provide answers to the clinical questions regarding the effect of red blood cell storage duration on subjects undergoing cardiac surgery.

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The authors reply:

We agree wholeheartedly with investigators of the Red Cell Storage Study trial (1) that the results from our study on fresh (4 hrs of storage) vs. stored (7 days of storage) rat blood in myocardial infarction should not be extrapolated to RBC transfusions to patients and this is also listed as one of the limitations of our study in the discussion (2). Blood storage duration is an unresolved but clinically important issue in blood transfusion in anemic patients. We applaud the efforts of investigators currently addressing this question by comparing the effects of different blood storage durations on patient outcomes in randomized clinical trials (1, 3, 4). It is well-known that there are major biological differences between rat and human erythrocytes. To this end, we have previously documented some of these storage-related differences (5); hence, our use of 7-day stored rat erythrocytes is more representative (but not equivalent) to human RBC stored for 4 wks. Other investigators have used xenograft models transfusing stored human RBC to rats (6). The strength of our model is that it allows us to measure

directly the effects of transfusion on tissue injury and generate hypothesis to be tested in clinical trials. However, extrapolation of any result found in animal studies to humans should be cautioned (7). We and other members of the transfusion community look forward to the results of randomized trials currently addressing the long-standing question regarding the clinical significance of RBC storage lesion (1, 3, 4).

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