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EDITORIAL: Safety of red blood cell substitutes as compared to stored donor red blood cells

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Red blood cell substitutes should be able to replace red blood cells (rbc) without causing more adverse effect than donor rbc. One of the safety concerns regarding rbc substitutes is related to vasoactivity. This problem has been greatly minimized by the removal of most of the tetrameric hemoglobin that causes vasoconstriction.

Recent reviews show that liberal blood transfusions has a 20% increase in mortality and a 56% increase in ischemic events when compared to restrictive strategies (1,2). The transfusion of stored packed rbc is also associated with an increase in ischemic coronary events (1,3). However, it has been suggested that this is only if transfusions were given when the hematocrits were more than 30% (4). Stamler's group shows that storage of donor blood for only 24 hour can lead to a marked decrease of the ability of rbc to effect hypoxic vasodilation (6). Their result suggests that storage of blood leads to rapid losses in NO bioactivity, and his is directly paralleled to decreases in the ability of rbc to effect hypoxic vasodilation. Valerie and Ragno in this issue report on how the effects of preserved red rbc can be related to the severe adverse events observed in patients infused with hemoglobin based oxygen carriers(6).

It is reasonable to require that rbc substitutes should be able to replace donor rbc without causing more adverse effect than donor rbc. On the other hand, is it reasonable to require that rbc substitutes should have no side effects while standard donor rbc are associated with adverse effects including ischemic coronary events ? It also follows from the paper by Valerie and Ragno in this issue that in clinical trials that involve the use of both blood substitutes and donor blood, it will be important to differentiate between the adverse effects caused by each of these two components.

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(3) Rao SV, Jollis JG, Harrington RA, Granger CB, Newby LK, Armstrong PW, Moliterno DJ, Lindblad L, Pieper K, Topol EJ Blood Transfusion in Patients With Acute Coronary Syndrome (2004) *J Am Med Assoc* 292:1555–1562.

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(5) James D. Reynolds, Gregory S. Ahearn, Michael Angelo, Jian Zhang, Fred Cobb, and Jonathan S. Stamler (2007). S-nitrosohemoglobin deficiency: A mechanism for loss of physiological activity in banked blood. *Proceedings National Academy of Sciences* 104: 17058–17062

(6) Robert Valeri and Gina Ragno (2008) The effects of preserved red blood cells on the severe adverse events observed in patients infused with hemoglobin based oxygen carriers. *Artificial Cells, Blood Substitutes & Biotechnology* 36: 3