

Nitric oxide could make blood transfusions safer

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Bags of blood collected during donation. Image: Wikipedia.

(Medical Xpress)—Blood transfusions are supposed to save lives. Doctors give transfusions to severely ill or injured people with the expectation that their conditions will improve. In fact, transfusions do not always help and can even make things worse. When red blood cells are stored, their ability to deliver oxygen decreases. This can cause tissue hypoxia in patients who receive blood transfusions, resulting in severe complications. In a study that appears in the *Proceedings of the National Academy of Sciences*, Jonathan Stamler of Case Western Reserve University in Cleveland and his colleagues show that adding nitric oxide to stored red blood cells improves oxygen delivery.

Red blood cells deliver oxygen to tissues throughout the body. A transfusion increases the amount of red blood cells in the body, which should, presumably, increase [oxygen delivery](#), improving tissue health.

However, the oxygen-carrying capacity of stored red blood cells decreases over time. Consequently, transfusions of stored blood can cause tissue hypoxia. Eventually, this can lead to heart attack, [kidney failure](#) or death.

Stamler and his team reasoned that a decrease in nitric oxide levels impairs the ability of banked [red blood cells](#) to deliver oxygen after transfusion. When nitric oxide attaches to [hemoglobin](#), it forms S-nitrosohemoglobin (SNO-Hb), which causes blood vessels to dilate, making it easier for oxygen to reach cells. When blood is stored, SNO-Hb levels decrease over time.

The researchers studied the effect of adding nitric oxide to banked blood, a process known as reinitrosylation, before using this blood in transfusions performed on mice, rats and sheep.

They performed top-up transfusions on mice using one-day-old and seven-day-old blood. After one day of storage, rodent blood loses more than 70% of its SNO-Hb. Mice that received reinitrosylated blood maintained normal [blood oxygen levels](#) in [skeletal muscle tissue](#). In comparison, oxygen levels declined in mice given untreated blood.

Stamler and his colleagues then tested the effect of reinitrosylation on blood transfusions performed on anemic rats. After removing between 25 and 30 percent of blood volume, the researchers performed transfusions, using either untreated or reinitrosylated stored blood. Oxygen levels in the muscle tissues of rats that received untreated blood remained low. However, rats receiving reinitrosylated blood experienced increases in tissue oxygen levels.

Studies of anemic sheep revealed similar results. Stamler's team anesthetized sheep two days after bloodletting and transfused them with 14-day-old blood. Treatment with reinitrosylated blood improved

vasodilation, blood flow to the kidneys and kidney function. Sheep that received transfusions of renitrosylated blood while remaining awake also experienced sustained improvements in oxygen delivery.

The team suggests that restoring levels of nitric oxide in banked blood would improve outcomes in human patients.

More information: S-nitrosylation therapy to improve oxygen delivery of banked blood, *PNAS*, Published online before print June 24, 2013, [doi: 10.1073/pnas.1306489110](https://doi.org/10.1073/pnas.1306489110)

Abstract

From the perspectives of disease transmission and sterility maintenance, the world's blood supplies are generally safe. However, in multiple clinical settings, red blood cell (RBC) transfusions are associated with adverse cardiovascular events and multiorgan injury. Because ~85 million units of blood are administered worldwide each year, transfusion-related morbidity and mortality is a major public health concern. Blood undergoes multiple biochemical changes during storage, but the relevance of these changes to unfavorable outcomes is unclear. Banked blood shows reduced levels of S-nitrosohemoglobin (SNO-Hb), which in turn impairs the ability of stored RBCs to effect hypoxic vasodilation. We therefore reasoned that transfusion of SNO-Hb-deficient blood may exacerbate, rather than correct, impairments in tissue oxygenation, and that restoration of SNO-Hb levels would improve transfusion efficacy. Notably in mice, administration of banked RBCs decreased skeletal muscle pO₂, but infusion of renitrosylated cells maintained tissue oxygenation. In rats, hemorrhage-induced reductions in muscle pO₂ were corrected by SNO-Hb-repleted RBCs, but not by control, stored RBCs. In anemic awake sheep, stored renitrosylated, but not control RBCs, produced sustained improvements in O₂ delivery; in anesthetized sheep, decrements in hemodynamic status, renal blood flow, and kidney function incurred following transfusion of banked blood were also

prevented by reinitrosylation. Collectively, our findings lend support to the idea that transfusions may be causally linked to ischemic events and suggest a simple approach to prevention (i.e., SNO-Hb repletion). If these data are replicated in clinical trials, reinitrosylation therapy could have significant therapeutic impact on the care of millions of patients.

[Press release](#)

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