

## Store donated blood for more than three weeks? Say NO (nitric oxide)

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Transfusion of donated blood more than three weeks old results in impaired blood vessel function, a new study of hospital patients shows. Blood banks now consider six weeks to be the maximum permitted storage time of blood for use in transfusion, but recent studies have suggested transfusing blood stored for more than a few weeks has adverse effects in patients undergoing cardiac surgery or critical care.

The new finding suggests a mechanism explaining why older blood might be detrimental to patient health: a deficiency in nitric oxide, a short-lived [chemical messenger](#) that relaxes blood vessels.

The results are being presented at the American College of Cardiology meeting in San Francisco. The presenter is cardiovascular research fellow Robert Neuman, MD. Senior authors include Arshed Quyyumi, MD, professor of medicine and director of the Emory Clinical Cardiovascular Research Institute, and John Roback, MD, PhD, associate professor of pathology and laboratory medicine and medical director of the Emory University Hospital blood bank.

In the current study, 43 patients at Emory University Hospital were set to receive cross-matched red [blood cells](#) for clinical indications. Members of the group were in hospital for various reasons, such as [cancer treatment](#) and surgery. They were randomly chosen to receive either fresh (less than ten days old) or aged (more than three weeks old) red blood cells. On average, they received the equivalent of two units. A unit is 450 milliliters of blood.

Neuman and his colleagues tested blood vessel function by measuring flow-mediated dilation (FMD). By ultrasound, they tested how much a blood vessel in the arm opens up after a blood pressure cuff is first tightened then removed. Flow-mediated dilation is an indicator of the health of the endothelial lining of the blood vessels and is a process that is dependent on nitric oxide.

Healthy, younger individuals can have flow-mediated dilation of up to 10 percent – the average for the hospitalized group was 5 percent. Patients receiving aged blood saw their FMD halved to 2.4 percent 24 hours after the transfusion, while patients receiving fresh blood saw no significant change in FMD.

This effect of older blood on blood vessel function is similar in size to that of eating a fatty meal (temporary), or the longterm effects of a cardiovascular disease risk factor such as smoking or diabetes.

Healthy flow-mediated dilation reflects sufficient production of nitric oxide, which is generated by the [blood vessels'](#) endothelial lining and causes them to relax. Nitric oxide is also important for delivery of oxygen by hemoglobin. Red blood cells carry nitric oxide bound to hemoglobin, and play a critical role in recycling the nitric oxide. Over time in storage, the nitric oxide is lost. Transfused red blood cells last a couple months in the patient. The Emory team did not measure FMD beyond 24 hours.

The so-called "red blood cell storage lesion" consists of several changes including oxidation, disruption of cellular structures, and loss of other chemicals such as the energy currency ATP and the hemoglobin regulator 2,3-diphosphoglycerate. A recent study has also shown that red blood cells stored for more than three weeks lose physical flexibility.

Thus, loss of nitric oxide is probably not the only important change, but

it may be significant in terms of effects on cardiovascular health, the authors argue.

"Aside from the direct infusion of nitric oxide-deficient blood, we may be also seeing an indirect effect from other aspects of storage that impact nitric oxide availability and endothelial function such as increased inflammation triggered by aged blood," Neuman says.

A 2008 study published in the New England Journal of Medicine found that [cardiac surgery](#) patients receiving older blood had a higher risk of dying in the hospital, and were more likely to need ventilation support or have sepsis or kidney failure. Two large-scale clinical trials (links below) are addressing the issue of the maximum time blood should be stored.

Although blood banks tend to use a "first-in, first-out" policy, limiting storage time could reduce the blood supply. One possibility could be to reserve fresh blood for those patients at most risk of cardiovascular problems, Neuman says.

Another way that nitric oxide deficiency could be remedied is with an additive such as nitrite, which the body uses as a storage reservoir for [nitric oxide](#), or some other preservative. [Red blood cells](#) are now stored in a solution with glucose, anticoagulant and acidity buffering properties.

"There is a lot of information that [blood](#) that has been stored for a while can cause problems for patients," Neuman says. "This starts to answer the question: what is causing the problem?"

**More information:** Clinical trials going on now addressing the blood storage time issue:

ABLE = age of blood evaluation

([www.ncbi.nlm.nih.gov/pubmed/21550205](http://www.ncbi.nlm.nih.gov/pubmed/21550205))

RECESS = red cell storage duration study  
([clinicaltrials.gov/show/NCT00991341](https://clinicaltrials.gov/show/NCT00991341))

Provided by Emory University

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