Team finds why stored transfusion blood may become less safe with age

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Transfused blood may need to be stored in a different way to prevent the breakdown of red blood cells that can lead to complications including infection, organ failure and death, say researchers at the University of Pittsburgh School of Medicine and Wake Forest University. This week in the early online version of *Circulation,* the team reports the latest findings from its ongoing exploration of the interaction between red blood cell breakdown products and nitric oxide (NO), revealing new biological mechanisms that can reduce blood flow and possibly damage vital tissues after administration of blood that has been stored for longer than 39 days.

In recent years, doctors have noted that transfusion of either many units of blood or of blood stored a long time may be associated with a greater frequency of complications, such as increased infection risk, kidney, lung or multi-organ failure and death, particularly among medically vulnerable patients, explained senior investigator Mark T. Gladwin, M.D., chief, Division of Pulmonary, Allergy and Critical Care Medicine, Pitt School of Medicine, and director of Pitt's Vascular Medicine Institute.

"When blood sits for a while, some of the cells break down and release their contents, which include molecules of hemoglobin and red blood cell microparticles," he said. "These accumulate in the stored bag of blood and are transfused into the patient with the blood. In the bloodstream, the hemoglobin and microparticles bind to and destroy NO, a very important molecule that is used by the body to keep blood vessels

dilated for normal blood flow."

The scavenging of NO causes blood vessel constriction that can prevent tissues and organs from getting adequate oxygen and activate the platelets and the coagulation system, as well as cause inflammation, Dr. Gladwin said.

From their experiments, he and his Wake Forest collaborators found that human blood stored under standard conditions accumulated "free" hemoglobin that was no longer contained in a cell and microparticles of damaged cells. Those breakdown products reacted with NO about 1,000 times more quickly than did intact red blood cells. Also, transfusion of even very low concentrations of hemoglobin caused blood vessel constriction and hypertension in a rat model.

"Avoiding the storage lesion, as it is referred to in our field, could require a new approach to how donor blood is stored prior to transfusion," said senior author Daniel B. Kim-Shapiro, Ph.D., professor of physics and director of the Translational Science Center at Wake Forest.

"Transfusion of stored blood is one of the most common medical therapies," he said. "By understanding the mechanism of the storage lesion, we can design methods to make blood transfusion safer. For example, perhaps we can restore nitric oxide activity that is lost upon transfusion, use preservation solutions that better limit the degradation of blood cells, or develop agents that scavenge free hemoglobin."

Other research projects are underway to find approaches to correct the problem, and to assess the safety of blood for transfusion that has been stored for longer than 14 days. Currently, federal guidelines allow transfusion of blood that has been stored for up to 42 days.

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