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Fresh Blood for Adults – Does it Matter?

Patient is a 44 y/o male in ICU with chest and pelvic injuries resulting from a motor vehicle accident. He has respiratory complications and remains on ventilator support. His current Hgb is 6.5 g/dL after receiving multiple transfusions, and he is not actively bleeding. The physician orders 1 unit of Red Blood Cells to be given today with a special request for "Less than 10 day old blood."

Is there rationale for transfusing "fresh" vs. "older" blood?

Over the past 2 decades, much discussion has occurred on storage of blood and whether transfusion of "older" Red Blood Cell (RBC) units is associated with worse patient outcomes. RBC products for transfusion have an expiration date of either 35 or 42 days depending on the preservative. Several highly provocative retrospective studies reported that transfusion of "older" RBC units is associated with increased mortality and morbidity; a nearly equal number of studies have reported no difference in clinical outcomes.[1-4] Recent published randomized control trials (RCT) are shedding light on the longstanding controversial question "Is fresh blood better?"[5-9]

What happens to red cells during storage?

The RBC membrane is a fluid structure which undergoes biochemical and shape changes during storage. As storage time increases the gradual changes in the RBC shape–biconcave disc to sphere (see Figure)–can lead to to reduced flow through blood vessels. The shape changes also result in release of potassium, free hemoglobin, iron, and bioactive substances. These changes, collectively known as the "storage lesion", are speculated to decrease oxygen delivery.

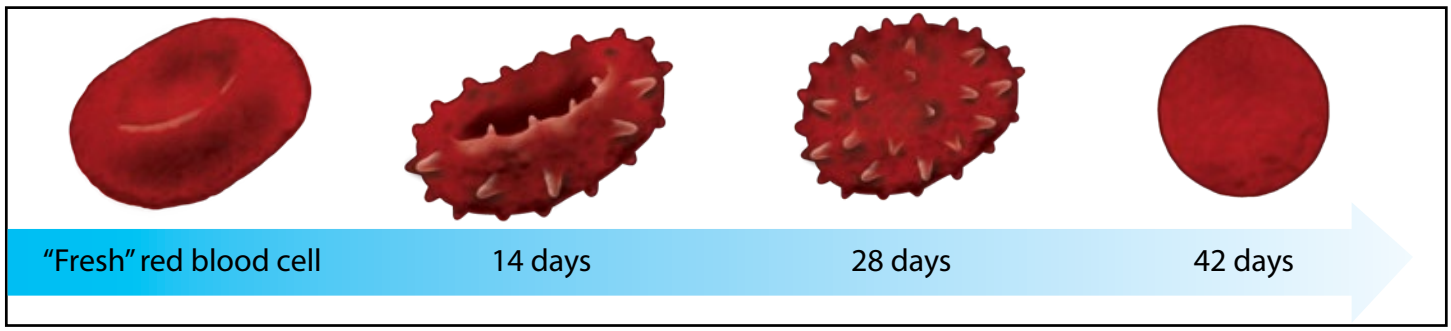
New Evidence from Recent Trials

Several recent major prospective RCTs involving acutely ill adult patients offer additional evidence on the long standing debate on age of blood for transfusion.

ABLE[5] (Age of Blood Evaluation Study): multicenter RCT in Canada and Europe involved 2,412 adult ICU patients. Patients were randomized to receive leukoreduced RBCs either as "fresh-blood" (less than 8 days old) or "standard blood" (oldest compatible unit available) with the first RBC transfusion request. Mean age of transfused RBCs was 6 days in the "fresh-blood" group vs. 22 days in the "standard blood" cohort. Primary outcome of death at 90 days was similar in both cohorts regardless of patient age, number of units transfused or APACHE-II score. No differences were observed in duration of respiratory, hemodynamic or renal support, or length of stay while in ICU or the hospital. The authors found no clinical benefit from transfusing fresher red cells to patients in the ICU.

RECESS[6] (Red-Cell Storage Duration Study): multicenter RCT in the US that studied the effect of RBC storage time on clinical outcomes in transfused cardiac surgery patients.

This study involved 1,098 patients 12 years or older undergoing complex cardiac surgical procedures. They were randomized to receive leukoreduced RBCs stored 10 days or less ("shorter-storage") or RBC



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units stored 21 days or longer ("longer-storage"). Mean age of RBCs at transfusion was 7.8 days (SD ±4.8) in the "shorter-storage" group vs. 28.3 days (SD ±6.7) in the "longer-storage" group. The authors found no difference in multi-organ dysfunction scores at postoperative day 7, serious adverse events, or mortality at day 28 between the two cohorts. The authors concluded that the "shorter-storage" RBCs were not superior to the "longer-storage" RBCs.

INFORM[7] (Informing Fresh vs. Old Red Cell Management Trial): multicenter international RCT investigated the effect of RBC storage on in-hospital mortality in more than 20,000 general hospitalized patients.

Subjects were randomized to either "short-term" storage (RBC unit with shortest time in inventory) or "long-term" storage (RBC unit with longest time in inventory) prior to receiving their first RBC transfusion. The demographics in both groups were similar as was the median number of RBC units transfused per patient (2 units; IQR 2-4). Mean age of blood in the short-term group was 13.0 days (SD ±7.6) and 23.6 days (SD ±8.9) in the long-term group. The study found no significant difference for in-hospital mortality between the two groups (9.1% vs. 8.7%) or in those patients considered as high-risk (cardiovascular surgery, ICU stay or oncology). The authors concluded that transfusion of longer storage RBCs was unlikely to result in an increased rate of death in the general hospital population.

TRANSFUSE[8] (Standard Issue Transfusion vs. Fresher Red Cell Use in Intensive Care): multicenter international RCT compared the effect of freshest available ("short-term") RBCs with standard issue ("long-term") RBCs on 90-day mortality.

Over 4,900 critically-ill adult patients with an anticipated ICU stay of at least 24 hours were randomized. Patient characteristics were similar in both groups with the exception of slightly older patients in the "short-term" cohort (mean 62.5±16.8 years vs. 61.4±17.3 years). Both groups had similar mean pretransfusion hemoglobin values and median number of RBCs transfused per patient. Mean RBC storage duration in the "short-term" group was 11.8 ±5.3 days compared to 22.4 ±7.5 days in the "long-term" group. Mortality at 90-days after randomization was 24.8% of patients in the "short-term" group vs. 24.1% in the "long-term" group. Secondary outcomes of ICU infection rate, ventilator time, renal-replacement support, and length of stay were comparable between the two groups. The authors concluded that transfusion of "short-term" storage RBCs provides no clinically meaningful benefit in critically-ill patients.

While the above studies involved adults, it is noteworthy to mention a recent single-center RCT (TOTAL[9]) involving children and age of blood. This study's unique design provides further evidence that RBC storage duration does not affect transfusion efficacy. In this trial the effect of RBC storage duration on oxygen delivery and overall tissue oxygenation, as measured by serum lactate levels, was evaluated among 290 children (age 6 months to 5 years) with severe anemia and high lactate levels. Improvement in serum lactate and overall tissue oxygenation was similar regardless if the child was transfused with an RBC unit stored 1-10 days ("shorter-storage") or 25-35 days ("longer-storage") from collection. Other outcomes such as adverse events, survival, and 30-day recovery were also not significantly different between the "shorter-storage" and "longer-storage" RBC groups.

Conclusions from these studies?

For the general medical and surgical adult hospitalized patient population, transfusion of fresh RBC units does not provide additional benefit over standard-issue practice. Current transfusion service practice of using "first in, first out" to provide RBC components does not need to change.

These studies did not include patients receiving chronic transfusion support. It is not known how the age of transfused red cell products could affect these patients.

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