Blood Donations, Blood Transfusions, and Iron

In the course of my book Dumping Iron, I discussed blood donations and some of their technicalities, specifically how they lower body iron stores. In this short article I’ll discuss a few more aspects of blood donations, blood transfusions, and iron.

Transfusion of old, stored blood is harmful

When blood is donated, it is mixed with an anticoagulant and a preservative. The former is to keep the blood from clotting, the latter to preserve its shelf life. Currently, donated blood has an expiration date 42 days (6 weeks) from the day it’s drawn. Most of the blood gets transfused well before its expiration date, but some does not, and gets transfused in the last week of its shelf life and up to the expiration date. This is especially true of less common blood types (B negative, say), for which the supply is lower.

When blood is stored, it ages, essentially decomposes. The red blood cells (RBCs) do not all become decrepit simultaneously, since they have different ages when they are donated. An average RBC lives about 120 days inside the body, before it’s destroyed and replaced with a new one. Hence, when a donor gives blood, the RBCs have a range of ages, from 1 to 120 days. As the blood ages inside its container, some of the RBCs get quite old indeed, well over 120 days, and they decompose (lyse) or otherwise decay.

If a patient is transfused with blood that’s been stored for 6 weeks, bad things can happen.

Red blood cells stored 35 days or more are associated with adverse outcomes in high-risk patients. There’s actually been a ton of research on this topic, but as this study is recent, I’ll just focus on this one.
Clinical trials have shown that longer red blood cell (RBC) storage duration does not worsen outcomes; however, these studies included few RBCs near the end of the 42-day storage limit. We tested the hypothesis that these “oldest” RBCs are associated with adverse outcomes.

The study looked at 28,247 transfused patients given 129,483 units of blood (RBCs, not plasma or platelets). They found that units of blood older than 5 weeks, but not those younger, were associated with adverse events. Odds ratio for mortality with older units of blood was 1.40 in critically ill patients— that means they were 40% more likely to die than those given younger units of blood. There was no extra mortality in those not critically ill, but in older patients there was increased morbidity (sickness) – 22% more likely to become ill.

A recent editorial on this matter concludes that “current maximum storage durations should be carefully reevaluated.” In other words, we’re storing blood too long, and the storage length should probably be no more than 35 days. The problem is that blood shortages are always ongoing, and that would further restrict the blood supply.

Why are old units of blood harmful? The editorial answers that “those that received blood stored for six weeks showed several effects associated with increased harm, including disruption in iron handling, increased extravascular hemolysis, and the formation of circulating non-transferrin-bound iron.”

Old blood cells lyse (similar to exploding) or otherwise decompose, and they release iron into the unit of blood, which when transfused gives the patient a large dose of iron. Some of the cells decompose after transfusion, also releasing iron.

Iron is the reason that transfusion of old blood can harm people.

While this may not seem relevant, if you or a family member need a transfusion, maybe you could inquire about (or insist on) blood that’s younger than 5 weeks old. That might save some agony. Some doctors used to order transfusions of the youngest blood possible in certain cases, though I don't know how common that practice is any longer.

Should the donation interval be longer?

Currently in the U.S., blood donors can give blood at 56 day (8 week) intervals. In my book, I mentioned that after a blood donation, the blood volume recovers quickly, possibly in 24 hours or less, as the body makes plasma to fill in the volume gap. But replacing the lost RBCs takes longer, hence the waiting period of 8 weeks until the next donation.

A recent study argues that this donation interval should be longer, due to iron requirements.
In conclusion, we provide detailed insights into changes and recovery in iron homeostasis over time until 180 days after blood donation in both regular and new whole blood donors. We conclude that for the vast majority of male donors, the donation interval of 56 days is too short to recover from donation-induced reduction in body iron stores. To stay on the safe side, we propose, as our expert opinion, that ferritin should be kept above 30 mg/L at all times. Based on our observations, this implies a baseline ferritin at each donation of at least 50 mg/L. Furthermore, we propose ferritin as the best parameter to assess personalized donation intervals because it (1) significantly decreases upon blood donation in the present study and (2) has been found to be associated with symptomatic ID in blood donors. Alternatively, and in the absence of point-of-care ferritin platforms, development of ID in donors may be prevented by (1) prolongation of donation intervals to 180 days in all donors as suggested by both the current and the REDS-III study and/or (2) (low) dose iron supplementation.

In a nutshell, they don’t want donors to become iron deficient, a laudable goal. We know from the data in my book that two donations annually almost guarantee having a ferritin in the desirable, low normal range, so that agrees with the study’s conclusion of 180 days between donations.

However, if someone starts with a ferritin on the high side, say >300, which many people have, it could take a long time to lower it given twice a year donations.

The authors also want donors to have enough time to get their iron stores back to where they were before, the very thing we’re trying to prevent.

My conclusion from this is that, if you are a regular blood donor who donates more than twice a year, you should be cognizant of your current ferritin level, in order to avoid iron deficiency.

A problem with taking the authors’ suggestion to the conclusion of lengthening donation intervals is the same one as with old blood: it would shrink the blood supply, probably even more than a shorter shelf life would. So it seems unlikely to happen.

A large national study of ferritin testing in Canadian blood donors found:

- Low-ferritin donors (ferritin <25 µg/L) represented 2.9% of first-time and reactivated (no donation in past 12 months) male donors, 32.2% of first-time and reactivated female donors, 41.6% of repeat male donors, and 65.1% of repeat female donors.

So, repeat donors were much more likely to have low ferritin, and especially the women. The study concluded:
The minimum hemoglobin level will be increased to 130 g/L for male donors [13 g/dl, that’s still a low number for men, below normal] and the minimum interdonation interval changed to 84 days (four donations yearly) for female donors based on iron deficiency risk groups.

If I’m reading that right, Canadian women can now donate only 4 times a year, instead of the previous 6 times. It also seems possible that many of the low-ferritin male donors would be found in the low hemoglobin group.

Previously, a minimum hemoglobin of 12.5 g/dl was required for both male and female donors, but just this past year, the American Red Cross raised the minimum for men to 13 g/dl. That should greatly ameliorate the problem of frequent male donors with iron deficiency. (I was also happy to see this statement from the Red Cross, “The Red Cross does not measure iron levels before blood donation. You can have a normal hemoglobin level and be accepted for blood donation, but still have a low iron level. The fingerstick that is done during your health history is a measure of your hemoglobin level.”)

**Recovery of hemoglobin after donation**

How long does it actually take to recover the RBCs, together with their hemoglobin, after a blood donation? Some researchers took a look at that.

**RESULTS:** After donation of approximately 550 mL of whole blood, [Note: larger than the American donation of 450 mL] the lost amount of tHb of 75 ± 15 g (8.8 ± 1.9%) was recovered after a mean of 36 ± 11 days (range, 20-59 days).

**CONCLUSIONS:** The results of this study confirm the minimal, recommended donation intervals (56 days for men) as adequate when, for the first time, judged upon by tHb as a direct marker of hematologic recovery.

The following chart shows the percentage of subjects, all of them men, average age 30, by how long it took each one to recover all lost hemoglobin after a donation.
About one fourth of them recovered completely in less than 25 days, and half by 35 days. Almost all recovered by just about the time until they could donate again, 56 days.

The human body makes 200 billion red blood cells daily – that’s 2.3 million per second, requiring $2 \times 10^{15}$ iron atoms each second. Unfathomable really. But that process speeds up after blood donation. If someone really needs to, and they have adequate iron stores, the body can ramp up production of blood up to 8-fold.

PS: Check out my books, Dumping Iron, Muscle Up, and Stop the Clock.
PPS: Check out my Supplements Buying Guide for Men.