

# TERUMO PENPOL REVIEW

ON BLOOD MANAGEMENT SYSTEMS

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## ***Blood donation, blood supply, iron deficiency and anemia – It is time to shift attention back to donor health***

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Since the 1980s blood collectors worldwide have focused on two central themes: blood product safety and an adequate blood supply. From the standpoint of safety, specifically the reduction of transfusion-transmitted diseases, the achievements over the past quarter century are remarkable. With respect to the adequacy of the blood supply, the past decade has witnessed major gains in some countries of Europe, Canada and the US and less

than had been expected in others, including Brazil, where the challenge of having a more stable blood supply, in which supply and demand are in better balance remains an important issue<sup>(1)</sup>.

On the other hand, the aforementioned achievement has come at a price: iron depletion of the repeat blood donor. Blood centers have long recognized that it is more effective and less expensive to collect blood from existing donors than to

recruit new donors. While first-time donors, particularly the young and minorities, have been more successfully recruited, 70% of US and 40-70% (depending on the region) of Brazilian donors are repeat donors<sup>(1,2)</sup>.

The only known significant disadvantage of blood donation is the potential risk of iron deficiency (ID). Iron is a vitally important element in the human metabolism. It plays a central role in erythropoiesis and is also involved in many other intracellular processes in all the tissues of the body. The potentiality of the individual donor to give blood without developing ID and iron deficiency anemia (IDA) varies widely, probably due to differences in nutritional iron intake, the differences in prevalences of ID in each study population, menstrual iron loss in females, the frequency of blood donation and the use of supplemental iron<sup>(2)</sup>.

The frequency of ID is high in blood donors (1.8% to 8.4% in males and 4.5% to 34.8% in females), and more dependent on the frequency of donations than on the cumulated number of

donations<sup>(2-4)</sup>. In addition to this, ID is a significant problem and its prevalence is increasing in many countries around the world. The prevalence has been reported to be 9-40% in women, depending on age and menstrual status and 2-5% in men<sup>(1,2)</sup>. Because menstruating females begin their blood donation careers from a lower starting point, subsequent donations pose a risk for greater clinical harm. Females have much higher rates of both ID and IDA.

The clinical implications of ID and IDA are not insignificant, including fatigue, reduced work performance and intellectual capacity, reduced endurance, restless leg syndrome, pica, and cognitive and immune function changes. The degree of symptomatology is proportionate to the severity of the anemia<sup>(1,2)</sup>.

Moreover, low hemoglobin (Hb) accounts for 4-10% of total deferrals, with the vast majority occurring in women. Therefore it seems reasonable to secure adequate iron reserves in the donor population in order to maintain an appropriate donation

potentiality and to avoid possible hematological and non-hematological complications related to ID<sup>(1,2)</sup>.

The question that arises is whether this practice is in the best interest of donor health. In this issue of *Revista Brasileira de Hematologia e Hemoterapia*, Silva et al., representing the Hemocentro Regional de Uberaba, Minas Gerais, Brazil, have brought this issue to light<sup>(5)</sup>.

Given the findings in this and other studies, what measures can blood collectors pursue to address iron depletion? There is no single answer, but several approaches should be considered: 1) modifying the donor Hb requirements and measurement of Hb, 2) changing the interdonation interval, 3) testing for serum ferritin, and 4) iron supplementation.

### **1. Modifying donor Hb requirements and measurement of Hb**

The current minimum Hb requirement in the Brazilian guidelines as well as in the European Union guidelines is 12.5 g/dL for females and 13.0 g/dL for males; these values seem to be reasonable<sup>(6,7)</sup>. However, we

know that IDA is the last stage of ID and it is evident that Hb measurement, alone, is inadequate to detect blood donors with ID but without anemia.

It is not surprising that the current practice results in accepting many iron-depleted female donors who have normal Hb values<sup>(2)</sup>.

Regarding measurement of Hb, Silva et al. demonstrated that there was significant discrepancy between the Hb measurements, with 38% previously considered unfit, presenting normal Hb levels by the automated method. They call the attention to the need for a more accurate control of Hb measurement techniques in order to reduce the number of blood donors deferred for low Hb levels.

### **2. Changing the interdonation interval**

With respect to the interdonation interval and iron status, the number of donations over the previous 2 years was the most significant indicator of ID and IDA in the RISE study<sup>(8)</sup>. For females, there were no significant differences in deferral rates if 15 weeks had elapsed since the last donation, but there were highly significant

differences between weeks 8 and 14. On the other hand, there was an insufficient number of males for evaluation. It is noteworthy that over time with successive donations the Hb decreased as well, such that the proportion of female donors with values below 12.5 g/dL, increased from 11% to 25%, while the men has a trend toward significance, with an increase from 1% to 5%. These findings highlight the point that the current standard of 8 weeks is insufficient to replenish iron stores<sup>(8)</sup>.

Thus, one option to mitigate the effects of blood donation on ID would be to increase the interdonation interval for donors of whole blood from the current eight weeks to at least 12 weeks. Such a change would have an impact on blood donor scheduling, but it is worth mentioning that several European countries, that recognized the anemia problem, limit annual whole blood donations (four and three for males and females, respectively) as well as to adopt the minimum interdonation interval of 12 weeks for whole blood<sup>(1,8)</sup>.

### **3. Testing for serum ferritin**

Assessing serum ferritin (SF) levels would be the most accurate way to assess “iron health”. However, testing for SF poses significant challenges. Besides being a moderately expensive test, collecting additional samples, determining the frequency of testing and handling donor counseling would need to be solved. Another drawback is that results are not readily available to make a decision on site<sup>(9)</sup>.

### **4. Iron supplementation**

Every blood donation (450+ 25 mL) is associated with significant iron loss, approximately 200 to 230 mg and the lost iron is not readily replenished. Even with iron-rich diets and excellent compliance, six months or longer are necessary to positively impact SF levels. Therefore, this practice is inadequate in the scenario of blood donation<sup>(2,9)</sup>.

Recent studies in blood donors have shown that short-term (4- to 8-week course) use of oral iron supplementation at 100-300 mg daily of elemental iron (and even utilizing lower doses such as 20-40 mg/day),

is effective in improving Hb levels, in replacing iron loss after blood donation even in menstruating females, in maintaining SF concentrations in a range of 50 to 80 g/L and significantly reducing blood donation deferral. Thus, low-dose iron administered (100 mg/day) for up to 60 days post-donation appears to be a sound and feasible strategy<sup>(10-12)</sup>.

### Conclusions and recommendations

The fact that blood donation results in iron depletion is old news to the transfusion medicine community and many recent studies stress how serious and prevalent ID is among blood donors. With greater appreciation of the clinical consequences of ID, both physical and intellectual, this issue must move to center stage and the transfusion medicine community has an obligation to address this matter.

While there is no question that the donor pool needs to be more robust to meet both current and future demand, concerns about the blood supply must take into consideration the donor health.

It is time to discuss more profoundly possible

approaches to address iron depletion in blood donors. It is time to shift attention back to donor health, which is indeed no less important than insuring a safe blood supply.

### References

1. Popovsky MA. Anemia, iron depletion, and the blood donor: it's time to work on the donor's behalf. *Transfusion*. 2012;52(4):688-92.
2. Caçado RD, Chiattonne CS, Alonso TT, Junior DML, Alves RCS. Iron deficiency in blood donors. *São Paulo Med J*. 2001;119(4):132-34.
3. Simon TL, Garry PJ, Hooper EM. Iron stores in blood donors evaluated by serum ferritin. *JAMA*. 1981;245(20):2038-43.
4. Pederson NS, Morling N. Iron studies in blood donors evaluated by serum ferritin. *Scand J Haematol*. 1978;20(1):70-6.
5. Silva MA, de Souza RA, Carlos AM, Soares S, Moraes-Souza H, Pereira GA. Etiology of anemia of blood donor candidates deferred by hematologic screening. *Rev Bras Hematol Hemoter*. 2012;34(5): 356-60
6. Brasil. Ministério da Saude. Agência Nacional de Vigilância Sanitária (Anvisa). Resolução RDC n. 57, de 17 de outubro de 2010. *Diário Oficial da União*. 2010 Dez 16. [cited 2012 Jul 5] Available from: <http://portal.anvisa.gov.br>
7. European Directorate for the Quality of Medicines & HealthCare. Guide to the preparation, use and quality assurance of blood components. 16th ed. Strasbourg: Council of Europe; 2010. p. 209-10.
8. Cable R, Glynn S, Kiss J, Mast AE, Steele WR, Murphy EL, Wright DJ, Sacher RA, Gottschall JL, Tobler LH, Simon TL; the NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II). Nemo GJ, Schulman J, King MR, Busch MP, Norris P, Cable RG, Rios JA,

Benjamin RJ, Roback JD, Sacher RA, Wilkinson SL, Carey PM, Murphy EL, Custer BS, Hirschler NV, Triulzi DJ, Kakaiya RM, Kiss JE, Gottschall JL, Mast AE; NHLBI Retrovirus Epidemiology Donor Study-II (REDS-II). Iron deficiency in blood donors: the REDS-II Donor Iron Status Evaluation (RISE) Study. *Transfusion* 2012;52(4):702-11. Comment in: *Transfusion*. 2012;52(6):1382-3; author reply 1383-5.

9. O'Meara A, Infanti L, Stebler C, Ruesch M, Sigle JP, Stern M, et al. The value of routine ferritin measurement in blood donors. *Transfusion*. 2011;51(10):2183-8.
10. Radtke H, Mayer B, Rocker L, Salama A, Kiesmetter H. Iron supplementation and 2-unit red blood cell aphaeresis: a randomized, double-blind, placebo-controlled study. *Transfusion*. 2004;44(10):1463-7.
11. Radtke H, Tegtmeier J, Rocker L, Salama A, Kieseewetter H. Daily doses of 20 mg of elemental iron compensate for iron lost in regular blood donors: a randomized, double-blind, placebo-controlled study. *Transfusion*. 2004;44(10):1427-32.
12. Pittori C, Buser A, Gasser UE, Sigle J, Job S, Rüesch M, et al. A pilot Iron Substitution Programme in female blood donors with iron deficiency without anaemia. *Vox Sang*. 2011;100(3):303-11.

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