

Are we bleeding our donors dry: Iron deficiency in blood donors



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Introduction

- The voluntary unpaid blood donation is a humanitarian act towards the sick by the healthy
- No transfusion service can survive without blood donors.
- The well being and health of the blood donors is of prime importance for the medical profession
- There are policies for protection of the recipients from the potential hazards of blood transfusion
- For protection of recipients screening of donors is mandatory but very little attention is given to the health status of donors

Introduction

- Early detection of blood disorders like G₆PD deficiency and sickle cell traits benefits both donors and recipients of blood products.
- Donors will benefit by proper guidance about the disorder
- Recipients will benefit by receiving good quality blood

Introduction

- Interval of 56 days between 2 donations was based on studies from the 1940s and 1950s, investigating recovery of Hb only
- Recent studies show that this interval is short and will lead to Iron Deficiency
- Testing for Hb alone will not be a marker for non-anemic Iron Deficiency and to prevent blood donors from developing Iron Deficiency

International hemoglobin standards for frequency of donation

Country	Hb- male g/dL	Hb-female g/dL	Donation frequency	
			Men	Women
Europe: Council of Europe	13.5	12.5	6x/yr	56 days; 4x/y
United Kingdom	13.5	12.5	84 days acceptable	112 days (R)
Scotland	13.5	12.5	3x/yr	
Germany	13.5	12.5	6x/yr	56 days
Sweden	13.5	12.5	4x/yr	84 days
Brazil	13.0	12.5	4x/yr	90 days
Hong Kong	13.0	11.5	4x/yr	3x/yr

International hemoglobin standards for frequency of donation

Country	Hb-male g/dL	Hb- female g/dL	Donation frequency	
			Men	Women
United States	12.5	12.5	56 days	
Canada	12.5	12.5	56 days	
Switzerland	12.5	12.5	4x/yr	3x/yr
France	13.0	12.0	6x/yr	56 days
Australia	13.0	12.0	84 days	
Israel	13.0	12.0	90 days 4x/yr	

Blood Products Advisory Committee (BPAC): September, 2008

Topic: Iron Status in Blood Donors

- Committee members agreed that iron depletion in blood donors is a concern.
- Discussed testing for iron status in the donor setting
- Discussed alternative strategies to mitigate iron depletion like:
 - ▣ Iron supplementation, dietary recommendations
 - ▣ Changing Hb/hct acceptance standards
 - ▣ Modification of interdonation interval

Iron in 450 ml blood

- One gram of haemoglobin contains 3.4 mg of iron
- In a normal individual with 15gm/dL of haemoglobin (100 ml of blood approximately 50 mg of iron)
- Removal of only 1 ml of blood = loss of 0.5 mg of iron
- In 450 ml of blood donated 225 mg of iron lost
- Donor has no iron deficiency, the erythrocytes and the haemoglobin level will generally return to normal within 3–4 weeks.
- So adequate iron stores are very important in maintenance of the donor health.

Kinetics of iron loss

- Iron loss is made up very quickly by mobilizing the iron stores in form of ferritin
- This is followed by replenishing the iron stores if diet is adequate.
- In donors with high frequency of blood donations their iron stores are under a constant pressure.
- In the absence of iron replacement this can lead to emptying of iron stores

Kinetics of iron loss in Male

- ❑ Frequency of iron deficiency in males 1.8 – 8.4%
- ❑ Storage iron: Adult males - approximately 1000 mg
- ❑ A twice/year blood donor loses about 600 mg
- ❑ Iron lost from a 450-ml donation (242 ± 17 mg) is made up in about 3 months by enhanced absorption of dietary iron

Kinetics of iron loss in Female

- ❑ Frequency of iron deficiency in females 4.5 – 34.8%
- ❑ Storage iron: Adult females- 250–500 mg
- ❑ Average menstruating woman loses about 650 ml/year.
- ❑ Almost 1.5 years would be required to replace iron lost at donation.

Factors which affect the low HB in a donor

- Difference in reference range for male and female and for different ethnic groups
- Difference in hemoglobin values obtained by capillary versus venous blood
- High prevalence of iron deficiency in women of child bearing age and frequent blood donors

Developmental Stages of Iron Deficiency (WHO)

A. Pre-latent

- Reduction in iron stores
- No reduction in serum iron levels
- HB, MCV, Transferrin saturation- normal
- Iron absorption increases
- Serum ferritin and marrow iron reduced
- No clinical manifestations

Developmental Stages of Iron Deficiency (WHO)....contd

B. Latent

- Iron stores exhausted
- Hemoglobin normal
- **Clinical signs of iron deficiency +/-**

C. Iron Deficiency Anemia

- Hemoglobin falls below the normal reference range
- Signs and symptoms of iron deficiency anemia present

Figure 5.2 Iron stores versus iron removed from donation. Source: Cook *et al* (2003).⁵³ Reproduced with permission of the American Society of Hematology.

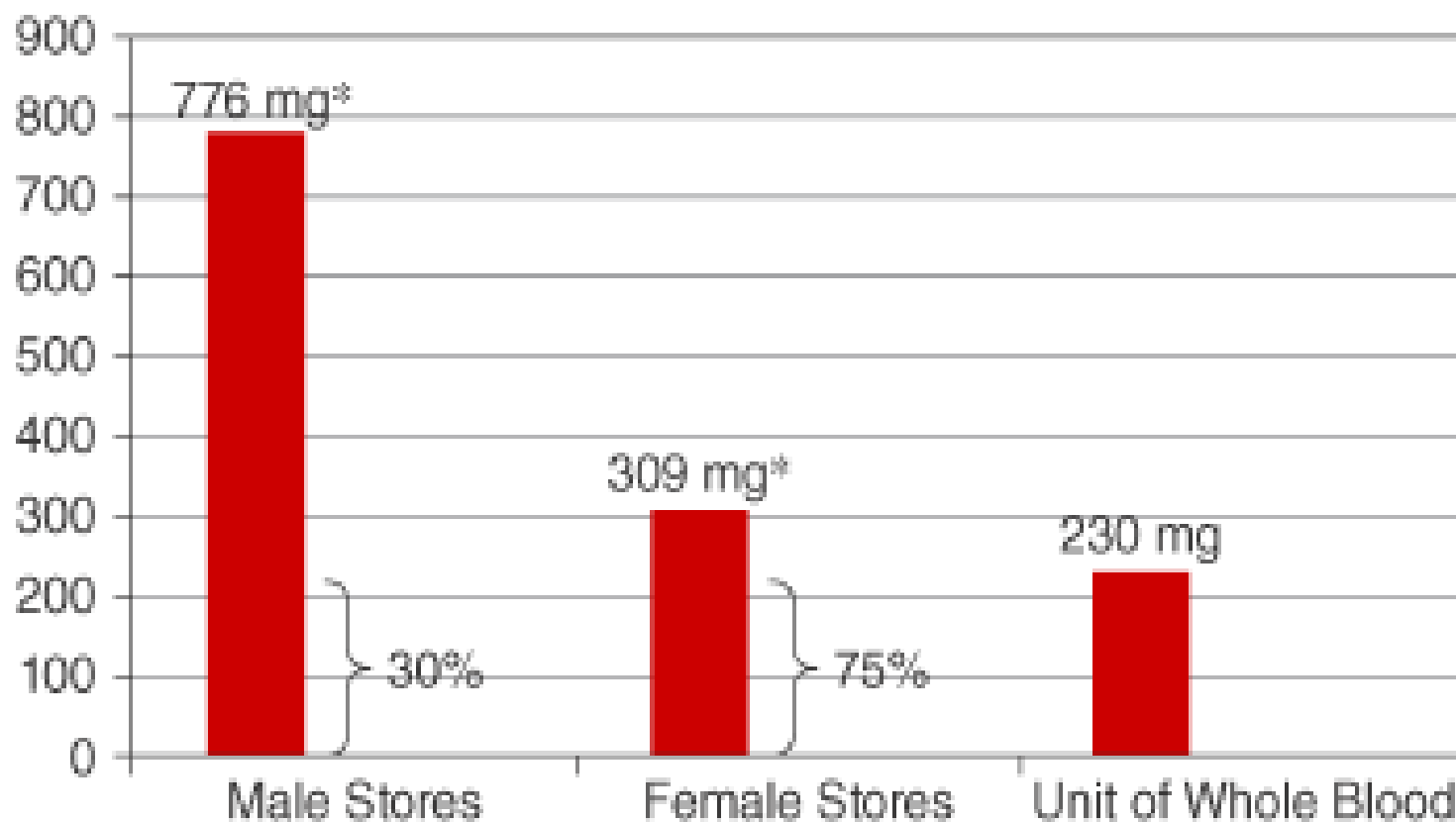
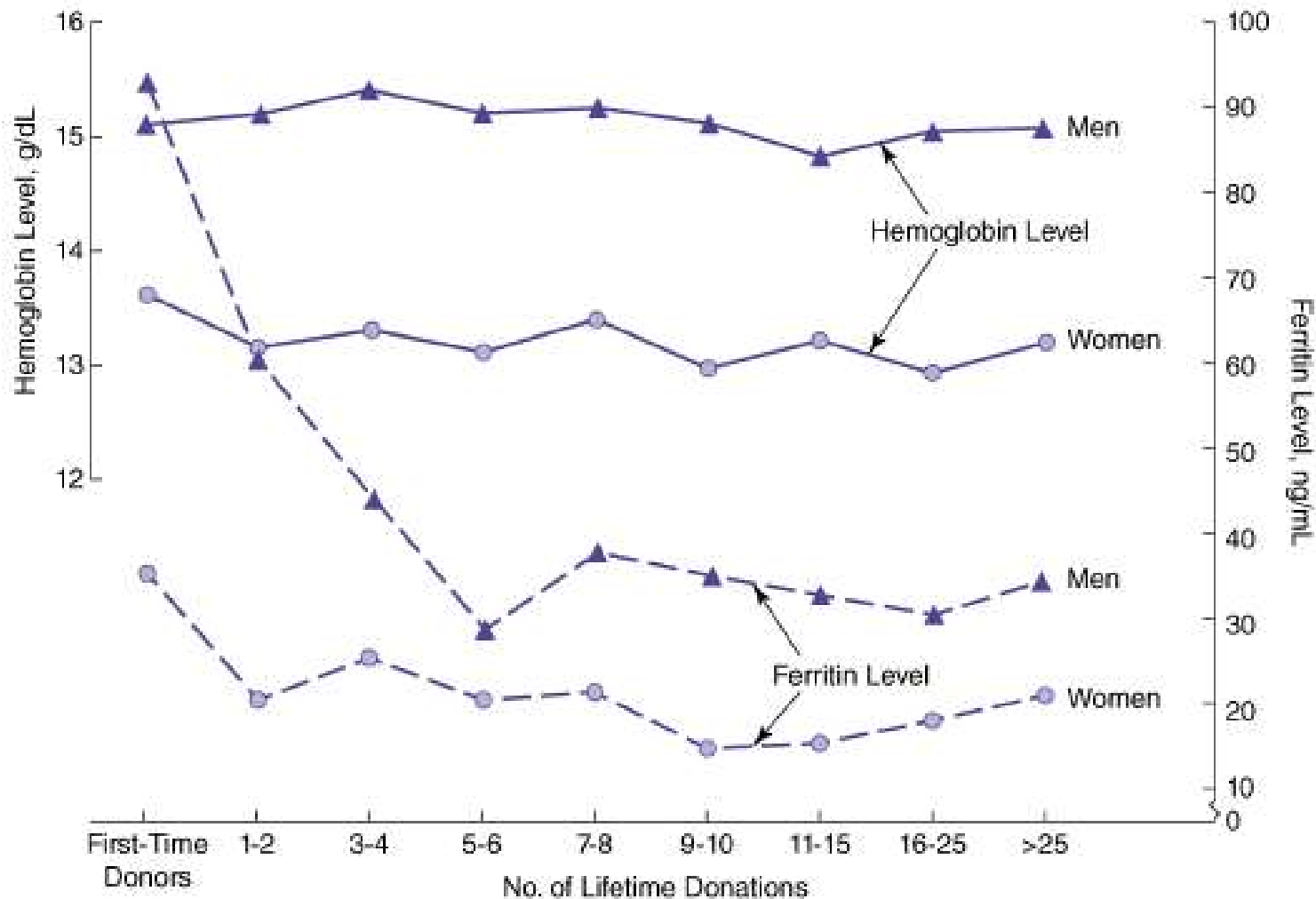


Figure 5.4 Changes in hemoglobin and ferritin with successive blood donations. ⁴⁶



Hb regeneration after normal blood donation

- In normal healthy subjects donate about 400 ml of blood (8% of their blood volume)
 - Circulating reticulocytes increased minimally and peaked on the **ninth day** after bleeding
 - The Hb level was lowest 1 or 2 weeks after bleeding, and increased rapidly thereafter, reaching predonation levels at **3–4 weeks**
- In a study in which total red cell volumes were measured in subjects who had donated about 190 ml of red cells, about 50 ml of red cells were restored after 1 week and restoration was almost complete at 6 weeks (*Heaton and Holme 1994*).

Rise Study - Predicting Iron Deficiency in Blood Donors

- REDS II Retroviral Epidemiological Donor Study is a multi-center research program funded by the National Heart, Lung and Blood Institute to conduct studies on the safety and adequacy of the blood supply
- RISE – REDS II Donor Iron Status Evaluation
- The REDS-II Donor Iron Status Evaluation (**RISE**) is a longitudinal study involving the six REDS-II centers which is designed to evaluate the effects of blood donation intensity on iron and hemoglobin status

RISE - Baseline Enrollment Data Collection

- **Hematologic and iron status markers:**
 - ▣ Fingertick hemoglobin or hematocrit
 - ▣ HemoCue venous hemoglobin
 - ▣ Plasma ferritin, sTfR (soluble transferrin receptor)
- **Iron protein polymorphisms:**
 - ▣ Transferrin polymorphism G277S
 - ▣ HFE (hemochromatosis) polymorphisms C282Y and H63D
- **Donor Questionnaire Data:**
 - ▣ Donation History: Lifetime; Past 1,2 years
 - ▣ Smoking: Lifetime, recent
 - ▣ Dietary Iron Consumption
 - ▣ Use of multivitamin/multiminerals and iron supplements
 - ▣ Aspirin use
 - ▣ For women only: Menstrual status/nature of periods; Detailed pregnancy history

Iron Depletion – 2 Levels

- Iron Deficient Erythropoiesis (IDE)

Begins with gradual loss of storage iron

Log soluble transferrin receptor/ferritin = / > 2.07

- Absent Iron Stores (AIS)

When iron stores are exhausted leads to AIS

Ferritin < 12ng/mL

Donors with Absent Iron Stores (AIS) and/or Iron Deficient Erythropoiesis (IDE) at Enrollment

Gender	Donor Status	AIS % ferritin <12 µg/L	IDE % Log (sTfR/F) ≥ 2.07
Females	FT/RA	6.5	24.6
	Fqnt	27.0	66.1
Males	FT/RA	0	2.5
	Fqnt	16.4	48.7

Laboratory monitoring of iron status

- In normal, well-nourished subjects, serum ferritin concentration is a good indicator of iron stores
- Red cell ferritin is affected only slightly by factors other than tissue iron stores
- Several studies of ferritin estimations in large series have confirmed that iron stores may be seriously depleted in blood donors (*Finch et al. 1977; Bodemann et al. 1984; Skikne 1984*).

Table 5.4 Assessment of Iron Status in Blood Donors

- Ferritin
- Soluble transferrin receptor (sTfR)
- Soluble transferrin receptor/ferritin ratio
- Zinc (Free Erythrocyte) Protoporphyrin (ZPP)
- Red blood cell parameters (HYPOm, CHr)

HYPOm % hypochromic mature RBC; CHr, hemoglobin content of reticulocytes.

For serial blood donors who have complete blood counts performed, a progressive drop in the red cell indices [mean cell volume (MCV), MCHC] provides an even easier and less expensive method of following functional iron status (*Leitman et al. 2003*)

Conclusions and Recommendations

- Iron deficiency among blood donors is an old fact
- Recent studies stresses on the importance and relevance of ID in blood donors
- Donor pool needs to be more robust so we should shift our attention back to donor health and discuss approaches to combat iron deficiency in blood donors

References

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**TIME TO
THINK**

