Blood Donor Iron Status
From Research to Policy

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Alberta Vein to Vein Conference
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Objectives

- To describe background relating to blood donation and iron
- To describe current research at Canadian Blood Services relating to ferritin
- To discuss current and future policy to mitigate iron deficiency caused by blood donation
Hemoglobin

- Oxygen transport protein that uses iron found in red blood cells.

- Normal range:
  - Male: 140-180 g/L
  - Female: 120-160 g/L (non-pregnant)

- A donor with a hemoglobin of less than 125 g/L is deferred.

Ferritin

- An intracellular protein that stores iron in a non-toxic form.
- Ferritin is used as a measure of iron status.
- Normal ~ 25-336 µg/L (or ng/mL), lower limit problematic
  Low ~ 13-24 µg/L (IDE)
  Absent < 12 µg/L (AIS)
Iron balance

- Iron stores 1,000 mg in males, 300 mg in females
- Daily baseline requirements 1 mg in males, 1.5 mg in pre-menopausal females
- Maximum dietary absorption 3.5 to 4 mg/day
Iron balance in blood donors

≈ 225-250 mg of iron

- In pre-menopausal women, iron stores will be depleted with 1 donation
- Donation volume is 500 ml 10%
- Hemoglobin (Hb) recovery to 80% of baseline takes 78-122 days on average with no iron supplementation
- Iron stores take even longer to recover

Kiss et al. HEIRS Study. JAMA 2015; 313:575
Why is iron balance important?

- Baseline iron levels
- Depleted iron stores (low ferritin)
- Drop in hemoglobin (Hb)
- Failed Hb, loss of donation
What are the consequences of low iron stores?

Iron is an essential trace element.
Iron deficiency may result in:
- Pica (urge to eat ice, other unusual substances)
- Restless leg syndrome
- Difficulty concentrating, learning
- Fatigue, low energy level
- Decreased physical endurance
Low iron stores in pregnancy

- In animal models, iron deficiency in pregnancy may affect fetal brain development
- Human studies are not as clear
- Women of childbearing age start out with low iron stores, and iron needs increase substantially in pregnancy
- Consequences of iron deficiency may be greatest in this group

Health consequences in otherwise healthy donors

- Few studies have been done in healthy, non-anemic donors

- A Danish study of over 16,000 non-anemic donors reported no association between iron status and self-reported mental or physical health.

Ferritin studies at Canadian Blood Services
2012 Study

- Initial study of ferritin levels in Ottawa donors, including donors accepted (n = 550) and deferred for low Hb (n = 50) in 2012
- Donors interviewed about diet, iron supplements, knowledge about iron needs
- Donors were informed of their ferritin level by letter and if low advised to see their physician
- Electronic survey and qualitative interviews after notification
- Monitor return rates

Transfusion 2014; 54:775
2014 Study
July 2014-December 2015

- Initial study demonstrated that iron deficiency was common in Ottawa donors
- A larger, more representative study was needed to assist in policy development
- All donors in the study donated a unit of blood
- Leftover sample was tested for ferritin concentration. About 80% of donations have adequate leftover sample to test.
Donors informed ferritin may be measured

Clinics selected

Retention samples retrieved, sent to National Testing Lab

Ferritin measured

Donor Hb, demographics extracted from database

Ferritin $\geq 25 \, \mu g/L$

No further action

Ferritin $< 25 \, \mu g/L$ or $> 336 \, \mu g/L$

Donor mailed letter, information sheet

Survey donors by email

Follow donation frequency, Hb
Study questions, 2014 ferritin study

- What are the risk factors for iron deficiency in a large, representative sample of our donors?
- Is it feasible to integrate ferritin testing and donor notification of low iron stores into routine operations?
- What is the impact of notification on donors:
  - satisfaction
  - hemoglobin (Hb)
  - actions
  - return rate
  - volume of calls from donors
Table 1  Hemoglobin and ferritin concentrations of whole blood donors in the study (July 2014-December 2015)

<table>
<thead>
<tr>
<th>Study donors</th>
<th>Females n = 5,640</th>
<th></th>
<th>Males n = 6,955</th>
<th></th>
<th>Total N = 12,595</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Hemoglobin g/L</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>125-129</td>
<td>889</td>
<td>16%</td>
<td>173</td>
<td>2.5%</td>
<td>1,062</td>
<td>8%</td>
</tr>
<tr>
<td>130-134</td>
<td>1,056</td>
<td>19%</td>
<td>302</td>
<td>4%</td>
<td>1,358</td>
<td>11%</td>
</tr>
<tr>
<td>≥ 135</td>
<td>3,678</td>
<td>64%</td>
<td>6,460</td>
<td>93%</td>
<td>10,138</td>
<td>81%</td>
</tr>
<tr>
<td>Ferritin (µg/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12</td>
<td>1,326</td>
<td>23.5%</td>
<td>824</td>
<td>12%</td>
<td>2,150</td>
<td>17%</td>
</tr>
<tr>
<td>12-24</td>
<td>1,721</td>
<td>30.5%</td>
<td>1,489</td>
<td>21%</td>
<td>3,210</td>
<td>25%</td>
</tr>
<tr>
<td>25-336</td>
<td>2,589</td>
<td>46%</td>
<td>4,540</td>
<td>65%</td>
<td>7,129</td>
<td>57%</td>
</tr>
<tr>
<td>≥ 337</td>
<td>4</td>
<td>0.1%</td>
<td>102</td>
<td>1.5%</td>
<td>106</td>
<td>1%</td>
</tr>
</tbody>
</table>
# Table 2  Ferritin levels of whole blood donors in the study by gender and donation frequency (July 2014-December 2015)

<table>
<thead>
<tr>
<th>Donation frequency past 12 months</th>
<th>N</th>
<th>Ferritin (µg/L) (%)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt; 12</td>
<td>12-24</td>
<td>25-336</td>
<td></td>
</tr>
<tr>
<td><strong>Females</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First time</td>
<td>713</td>
<td>76 (11)</td>
<td>184 (26)</td>
<td>450 (63)</td>
<td></td>
</tr>
<tr>
<td>Reactivated*</td>
<td>1,186</td>
<td>84 (7)</td>
<td>268 (23)</td>
<td>834 (70)</td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>2,951</td>
<td>849 (29)</td>
<td>968 (33)</td>
<td>1,133 (38)</td>
<td></td>
</tr>
<tr>
<td>≥ 4</td>
<td>790</td>
<td>317 (40)</td>
<td>301 (38)</td>
<td>172 (22)</td>
<td></td>
</tr>
<tr>
<td><strong>Males†</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First time</td>
<td>545</td>
<td>4 (0.7)</td>
<td>9 (1.7)</td>
<td>493 (90.5)</td>
<td></td>
</tr>
<tr>
<td>Reactivated*</td>
<td>957</td>
<td>4 (0.4)</td>
<td>26 (2.7)</td>
<td>898 (94)</td>
<td></td>
</tr>
<tr>
<td>1-3</td>
<td>3,286</td>
<td>225 (7)</td>
<td>664 (20)</td>
<td>2,367 (72)</td>
<td></td>
</tr>
<tr>
<td>≥ 4</td>
<td>2,166</td>
<td>591 (27)</td>
<td>789 (36)</td>
<td>782 (36)</td>
<td></td>
</tr>
</tbody>
</table>

* No donation in > 12 months
† 102 males (1.5%) and 4 females (0.07%) had ferritin > 336 µg/L
ELECTRONIC SURVEY

6 months post-notification of low ferritin result

n=899 (57% response rate)
## Response to low ferritin result

<table>
<thead>
<tr>
<th>Received letter about ferritin</th>
<th>96%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surprised</td>
<td>46%</td>
</tr>
<tr>
<td>Neutral</td>
<td>22%</td>
</tr>
<tr>
<td>Not surprised</td>
<td>32%</td>
</tr>
<tr>
<td><strong>Results were useful</strong></td>
<td>64%</td>
</tr>
<tr>
<td>Neutral</td>
<td>23%</td>
</tr>
<tr>
<td>Results not useful</td>
<td>13%</td>
</tr>
<tr>
<td><strong>Tried to find out more about ferritin</strong></td>
<td>72%</td>
</tr>
<tr>
<td>Donor’s physician</td>
<td>48%</td>
</tr>
<tr>
<td>Own website search</td>
<td>29%</td>
</tr>
<tr>
<td>Canadian Blood Services website</td>
<td>10%</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>9%</td>
</tr>
<tr>
<td><strong>Canadian Blood Services should be testing for ferritin?</strong></td>
<td>92%</td>
</tr>
<tr>
<td><strong>Will return to donate</strong></td>
<td>88%</td>
</tr>
</tbody>
</table>
How clearly do you understand the difference between ferritin (iron stores) and hemoglobin?

- Very clear: 38%
- Neutral: 21%
- Not clear: 41%
Actions Taken After Receiving Letter

Saw a physician 63%
   +8% with scheduled appointment

Saw a pharmacist 20%
   +6% plan to

Taking iron supplement 60%
   80% started after receiving results

Taking multivitamin with iron 40%
   47% started after receiving result

Changed diet to include more iron 31%
   87% started after receiving result
Figure 1  Number of donations given by female donors with low ferritin 2 years before and after the index donation.
Figure 2  Number of donations given by female donors with normal ferritin 2 years before and after their index donation
Qualitative study

- Aims to assess the long term impact of ferritin testing on our donors, and lend insight into answers to electronic survey.

- 47 donors were contacted by email from May 2014 to June 2014, and were asked to participate in a voluntary, loosely scripted qualitative telephone interview.

- 21 donors completed the interview (45% response rate). Interviews ranged from 5 to 15 minutes.

- Using the grounded theory, the qualitative data was assessed and coded.
Themes

Visit to Physician

Comprehension of Ferritin

Iron Supplements

Donation Behaviours

Diet
Many donors did not book an appointment with their physician upon learning the results, but had discussed the issue at their subsequent annual check up.

A few donors expressed that their physicians were puzzled about the results and questioned their accuracy.

Some donors were dissatisfied with the way in which their physicians were managing the issue.

Although the donors received follow up, some only had one subsequent blood test and were not notified of their results.

Interviewer: Okay and would you be able to tell me a bit about how that went?
Respondent: Not that well...well I brought, I think I had a letter with me, and so I brought that in and showed it to her and she just, honestly she just kind of scoffed and said that wasn’t really a good measure of things and at the time it was during my checkup so she did give me one of those requisitions for the blood test, you know you get tested for all sorts of things, and admittedly I never got around to going for those tests.

(Female, Age 51, Repeat Donor-Deferred for low Hb at time of 2012 study)
Iron Supplementation

- Majority of donors received additional recommendations from their physicians to begin taking iron supplements.

- Approximately half abandoned the practice after a few weeks or months.

- Chief reasons for discontinuing:
  - Negative side effects
  - Perception that supplement made no difference

Interviewer: Do you still currently take a supplement?
Respondent: No I do not.

Interviewer: And when you were taking the supplement, were you taking it daily?
Respondent: I was, uh, trying to take it daily. Unfortunately it was making me feel quite nauseated so I probably only made it one week when I had to stop.

(Female, Age 43, Repeat Donor-Deferred for low Hb at time of 2012 study)
Iron Supplementation

Of concern, is the number of donors (43%) that are taking the iron supplement inappropriately.

Interviewer: So your doctor suggested taking the iron supplement then?
Respondent: Yes.

Interviewer: Do you currently still take the iron supplement?
Respondent: Um, only if I feel I need to, I try to watch my diet better.

Interviewer: And “when you feel like you need to” is that only when you’re feeling tired then and you take one?
D: Yeah.

(Female, Age 61, Repeat Donor)
Diet

- Half of the donors attempted to make a positive change to their diet and have continued to do so.
- They now eat meat or green leafy vegetables once a week and are much more aware of their diet in regards to iron.
- Additional positive changes:
  - Checking nutritional labels regularly for iron content
  - Discussing issue with family members
  - Doing research
- Prefer modifying diet over taking supplements
- Chief reasons for no change:
  - Already had an iron rich diet
  - Did not enjoy eating foods that were high in iron

Respondent: Um, I changed my diet mainly because I needed to change my diet so gone more away from basically protein based diet more to eating Canada food guide requirements. I’ve noticed a health change, a weight loss, and I, you know, feeling more energy etc. And I’ve also cut out alcohol immensely.

Interviewer: That’s good. Um, are you conscientious at all in your diet about the iron you include?

Respondent: Um, I try to make sure I’m getting at least four times a week a decent serving of iron based foods.

(Male, Age 51, Repeat Donor)
More than half of the donors (76%) decided to change their donation behaviours.
- Lengthen time between donations
- Discontinue donating entirely
- Hoping to resume donating in the future

Most of these decisions were made independently

A few donors continue to donate every 56 days and are not concerned with the issue or do not understand what ferritin is.

Interviewer: So are you thinking about continuing donating now that your levels are normal?
Respondent: I'll probably slow it down significantly. Maybe like once a year.

Interviewer: And is this reduction attributable to the low ferritin?
Respondent: Yes.

(Male, Age 24, Repeat Donor-Deferred for low Hb at time of 2012 study)
Donor Comprehension of Ferritin Result

- Many donors do not understand what ferritin is (often confused with hemoglobin).
- Many donors admitted that their conversation was very brief and they did not know the difference between the two.
- Some donors were willing to do research on the issue.
- Other donors were completely unaware of the difference and consequently it seemed as though they were having some difficulty understanding the purpose of the study.
Results
Do Donors Want to Know Their Ferritin Level?

- Mixed thoughts:
  - More aware but not overly concerned (not a fatal issue)
  - Positive changes (being proactive to improve health)
  - Motivated to revisit issue
  - Grateful due to additional precautionary testing (colonoscopy, endoscopy etc.)

Interviewer: No, okay. Would you say you’re more conscientious about your iron status at all?

Respondent: In the back of my mind yeah, but no (laughing). Does that make sense? Like having these results didn’t make me worry about the future of my health it was like oh I guess I need to get more on the iron input but never really thought oh my goodness I’m dying because I have an iron deficiency.

(Male, Age 51, Repeat Donor)
Learnings from Ferritin Studies

- Iron deficiency is common in our whole blood donors, risks are:
  - Female gender
  - Frequency

- Low Hb is not a good predictor of low ferritin

- The majority of donors say ferritin testing should be done, and are willing to take action

- Donors have poor understanding of iron status and of which actions are appropriate

- This may limit effectiveness of interventions
So what can we do about it?

Iron Status

- Lengthen interdonation interval
- Increase minimum hemoglobin criteria
- Provide iron supplements
- Ferritin testing and notification
- Donor education about iron loss from donation

So what can we do about it?
Current Status

- Minimum hemoglobin is 125 g/L for males and females
- Low Hemoglobin deferral is 56 days
- Donor Education Materials have been enhanced
  - pamphlet
  - information sheets
  - web site
- Encourage younger female donors (17-24) to rebook at 112 day intervals (3 times/yr)
Anticipated Changes (near future)

- The minimum hemoglobin for males will increase from 125 g/L to 130 g/L
- Female whole blood donors - interdonation interval will increase from 56 days to 84 days (maximum 4 donations per year)
Possible Options in the Long Term

- Further modification of interdonation intervals
- Introduction of selective ferritin testing in an operational context
- Further refinement of donor rebooking strategy, based on donor hemoglobin or ferritin results
From Research to Practice

- Studies of our own donors inform policy
- Interventions can be oriented towards our operational environment and the Canadian context
- permits identifications of areas where more attention may improve compliance (eg. donor education, multi-pronged approach)
- Ensures we have a good base of data and methodology to monitor the impact of policy and modify as appropriate
Thank-you!

Study team:

MINDY GOLDMAN (PI)
Vito Scalia
Jenna Scalia
Samra Uzicanin
Lori Osmond
Jennifer Cuffari

Other Canadian Blood Services groups:

National Testing lab
Donor testing labs
National Contact Centre
Medical Offices

Donors for participating