

**YOU COULD SAVE
A LIFE LIKE LILY'S**



Donor Haemovigilance

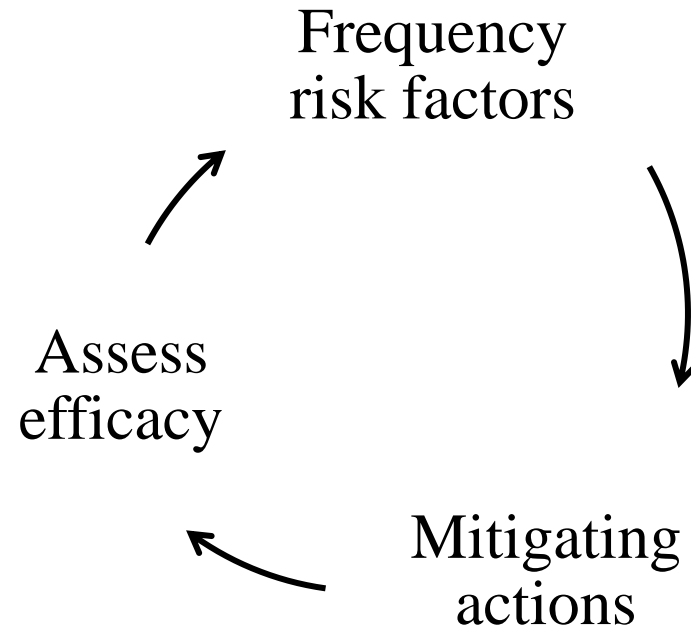


**Mindy Goldman MD
Canadian Blood Services
15th International Haemovigilance Seminar
Feb 20, 2013
Brussels, Belgium**

Why is donor vigilance important?

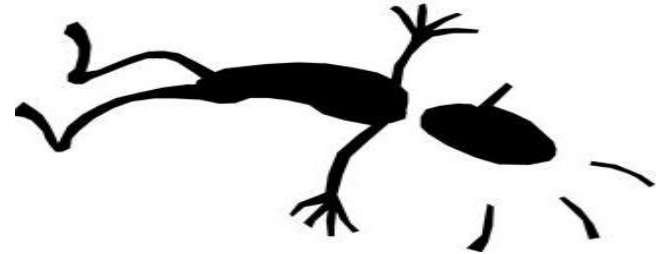
- Donor harm
 - injury, long term health effects
- Loss of donations and donors
 - inadequate collections
 - nonreturn or deferral
- Reputational risk
 - legal claims
 - NOT likely to encourage others to donate

Goals of donor haemovigilance



Donor adverse events

- Acute - at time of donation or shortly after donation
 - local arm complications (bruising, nerve injury)
 - vasovagal reactions (prefaint, faint)



- Long-term - cumulative
 - iron depletion



Vasovagal reactions

- Range of symptoms from feeling weak → loss of consciousness
- 2 main mechanisms
 - physiologic – effect of volume loss
 - psychologic – change in vagal tone
- Mild reactions occur in 2-5% of donors
- Loss of consciousness occurs in ~1 in 1,000 donations

Frequency of vasovagal reactions

- Lack of standardisation of definitions and classification
- Varying interpretation of definitions by clinic personnel
- Inadequate capture of reactions occurring off clinic
- Hidden reason for donor nonreturn



Classify this reaction

- 17 year old Mini Ma
- First time donor
- Starts looking pale, sweaty during donation
- Feels light-headed
- Rapid pulse noted
- Immediately after donation, BP = 90/60
- Much better after resting for 40 minutes on the bleeding chair



US Biovigilance System

Reaction Type	Category	Signs and Symptoms
Vasovagal	Prefaint, no LOC (uncomplicated or minor)	<ol style="list-style-type: none">1. Cold extremities, chills2. Feeling of warmth3. Hypotension4. Lightheaded/Dizziness5. Nausea/vomiting6. Normal pulse7. Pallor, pale skin or lips8. Rapid pulse9. Slow pulse10. Sweating11. Twitching12. Weakness

US Biovigilance System

Reaction Type	Category	Signs and Symptoms
Vasovagal	LOC, any duration (uncomplicated)	<ol style="list-style-type: none">1. Cold extremities, chills2. Feeling of warmth3. Hypotension4. Lightheaded/Dizziness5. Loss of consciousness < 60 seconds6. Nausea/vomiting7. Normal pulse8. Pallor, pale skin or lips9. Rapid pulse10. Slow pulse11. Sweating12. Twitching13. Weakness

US Biovigilance System

Reaction type	Category	Signs and Symptoms
Vasovagal	LOC, any duration (complicated)	<ol style="list-style-type: none">1. Chest pain2. Cold extremities, chills3. Convulsions4. Feeling of warmth5. Hypotension6. Lightheaded/Dizziness7. Loss of bladder, bowel control8. Loss of consciousness < 60 seconds9. Loss of consciousness >= 60 seconds10. Nausea/vomiting11. Normal pulse12. Pallor, pale skin or lips13. Rapid pulse14. Slow pulse15. Sweating16. Tetany17. Twitching18. Weakness

ISBT/European Haemovigilance Network

- Mild reaction – subjective symptoms only
- **Moderate reaction – objective symptoms**
- Severe reaction – hospitalization, or significant disability or incapacity following a complication
- Mini Ma does not meet minimal age criteria!

UK

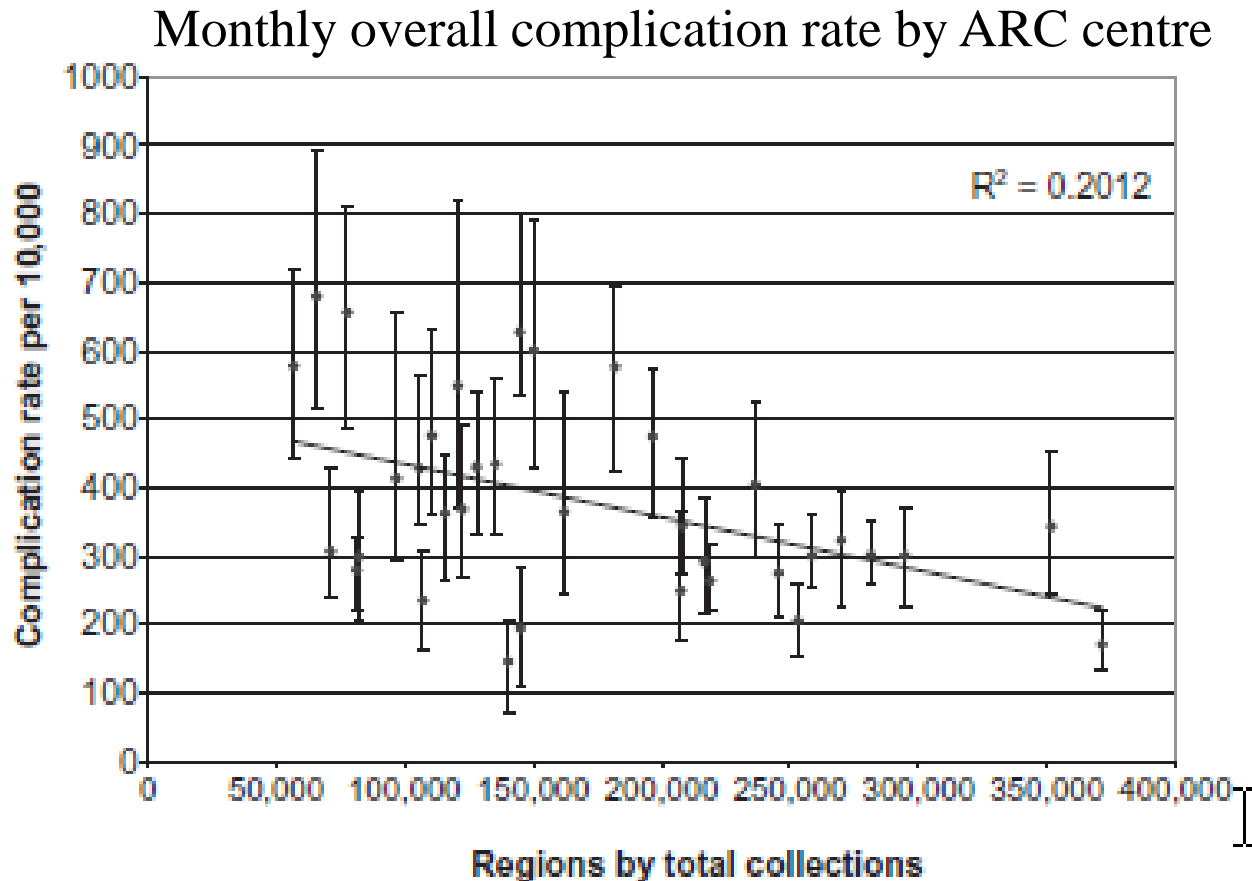
- **Grade 1 - no loss of consciousness**
- Grade 2 - loss of consciousness
- Grade 3 - loss of consciousness with added complications

Canadian Blood Services

- Mild reaction - **no loss of consciousness**
 - resolves < 15 minutes
- Moderate reaction - brief loss of consciousness (< 30 seconds)
 - full recovery < 30 minutes
- Severe reaction - longer loss of consciousness (> 30 seconds)
 - **prolonged recovery > 30 minutes**



Variability in interpretation by clinic staff



Eder et al
Transfusion 2008; 48:1809

Reactions occurring off clinic

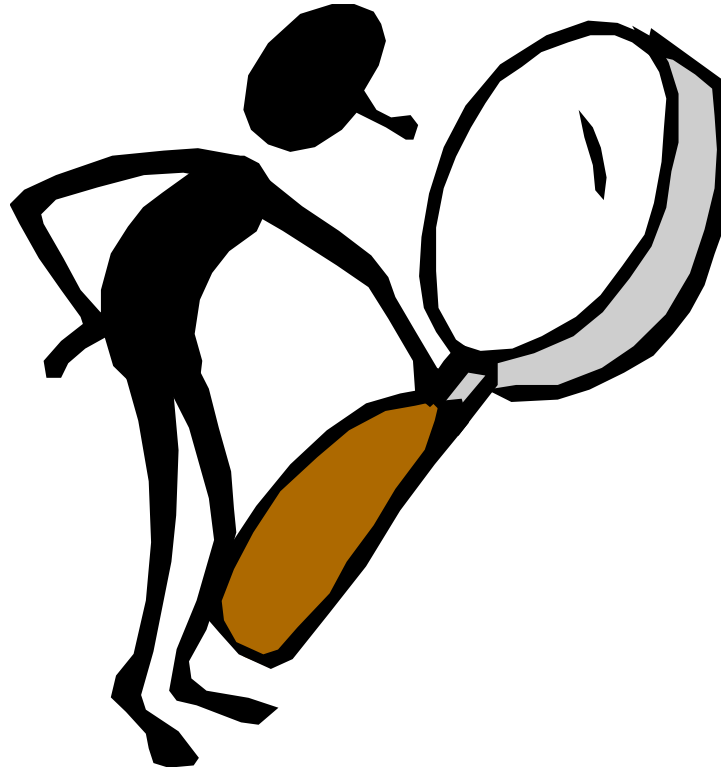
- Are more likely to result in falls, head trauma, and other injury
- Are often not reported to the blood centre, since rates on post-donation interviews or surveys are 2-5 times higher than reported rates
- In CBS anonymous donor survey, only 51% of donors who sought outside medical advice also call blood centre

Kamel et al. Transfusion 2010; 50:556

Newman et al. Transfusion 2003; 43:598

Goldman et al. Transfusion; Epub Dec/2012

Recent developments, vasovagal reactions



Identification of risk factors for vasovagal reactions

- Focus on younger donors
- Major risk factors
 - 1st time donor
 - younger age
 - low estimated blood volume (EBV)
 - female gender

Wiltbank et al. Transfusion 2008; 48:1799
Eder et al. Transfusion 2011; 51:1522
AABB Association Bulletin 08-04



Trials of preventative measures

- Volume loading pre-donation
- Applied muscle tension
- Salty snacks
- Better pre-donation education materials



Van der Berg et al. Transfusion 2012; 52:2577

Ditto B et al. Transfusion 2007; 47:2217

Reassessment of criteria to protect the donor

- More stringent height and weight (EBV) criteria for younger donors
- Donor blood pressure and pulse
- Upper age limit
- Chronic medical conditions (diabetes, cardiovascular disease)
- Medications



Shift to evidence-based criteria

- Criteria for many medical conditions based on “common sense”
- With an aging population, these criteria may lead to increasing donor deferrals in the future
- Variability in practice points to the absence of evidence behind many criteria

Eder et al. Transfus Med Rev 2009 (23):205

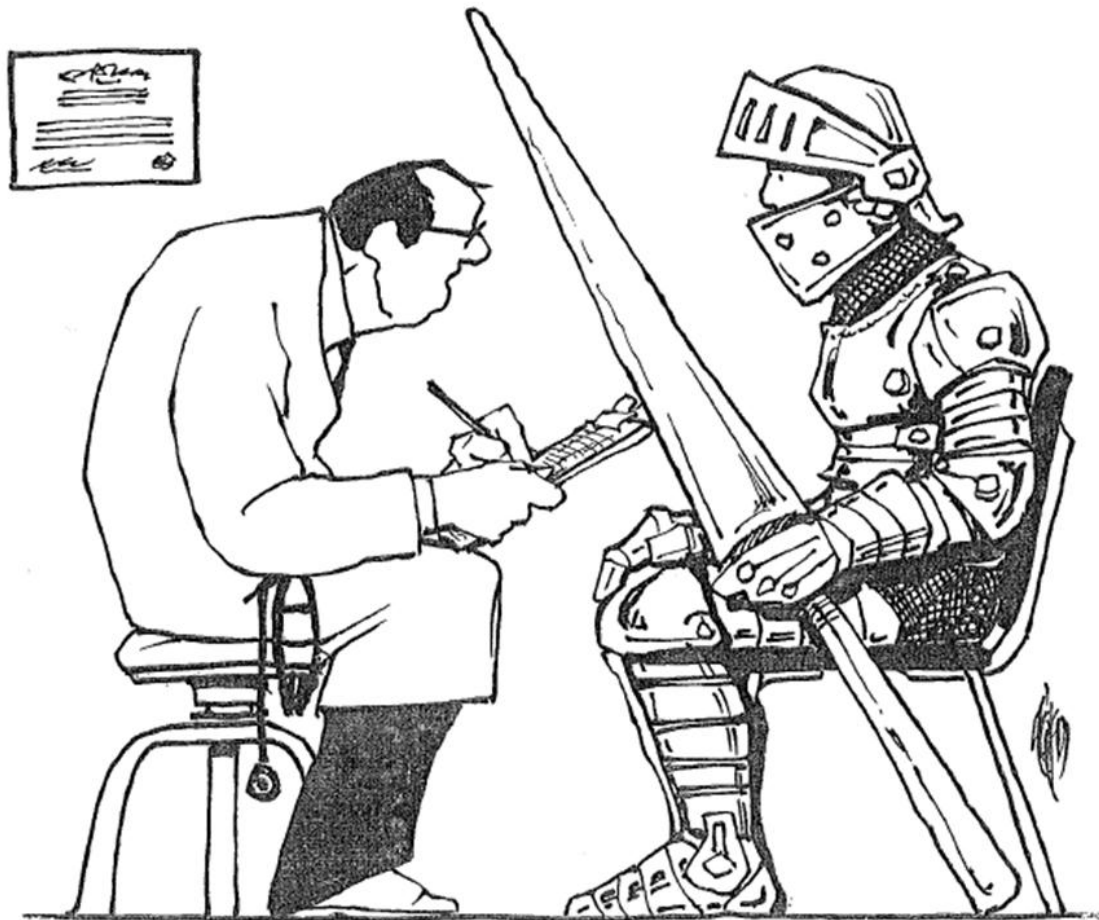
Evidence to assess criteria

- Analysis of risk factors for adverse donor events, current criteria
- Analysis of adverse events in autologous donors, less restrictive criteria
- Surveillance of complication rates before and after changes
- International comparisons

DONOR VIGILANCE!



Blood donors and iron status



"Are you getting enough iron?"



Canadian Blood Services
it's in you to give

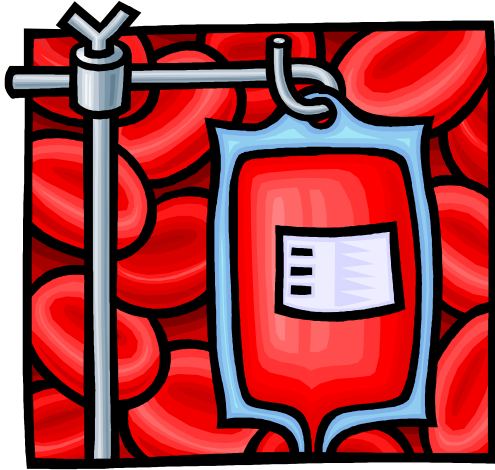
Iron balance

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



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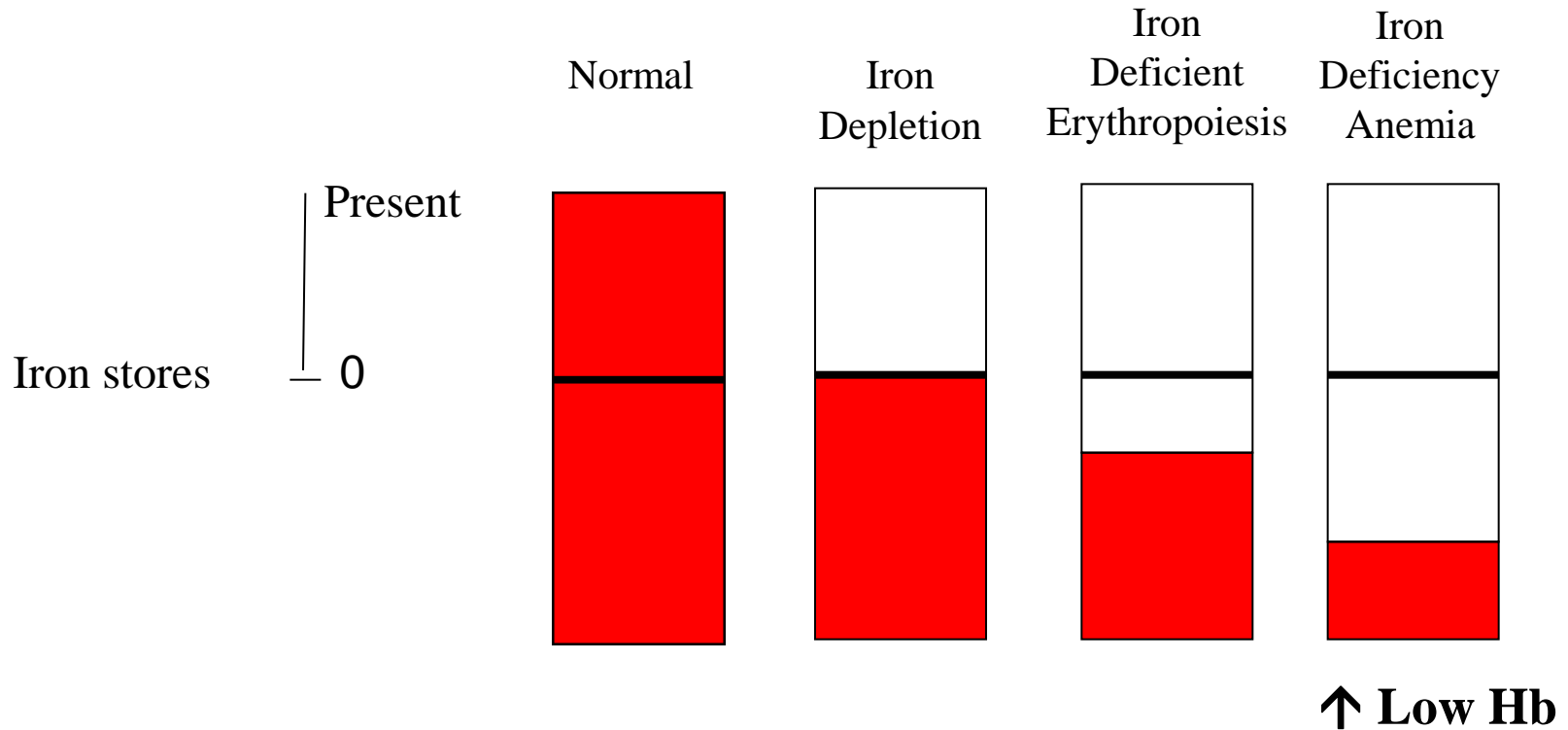
Iron balance in blood donors



$\approx 225\text{-}250$ mg of iron

- Donation volume is $500\text{ ml} \pm 10\%$
- In pre-menopausal women, iron stores will be depleted with 1 donation
- It will take 90 days of maximal iron absorption to replenish iron lost
- Smaller volume collections will cause less iron loss

Assessing iron deficiency



Assessing iron deficiency

- Storage iron is usually estimated by plasma ferritin levels
- Normal levels range from 24-336 $\mu\text{g/L}$ (or ng/ml)
- Levels $< 12 \mu\text{g/L}$ specific but not sensitive
- $\text{Log (sTfR/ferritin)} > 2.07$ is more sensitive for iron-deficiency erythropoiesis
- Zinc protoporphyrin/heme ratio (ZnPP/H) has been used
- A whole blood donation would cause a drop of ferritin level of $\approx 30 \mu\text{g/L}$

What are the consequences of low iron stores?

- 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
- Few studies have been done in otherwise healthy, nonanemic donors



International whole blood donation criteria

Jurisdiction	Hemoglobin (g/L)		Minimum interval (days)		Maximum donations per year	
	Males	Females	Males	Females	Males	Females
US	125	125	56	56	7	7
Canada	125	125	56	56	7	7
Australia	130	120	84	84	5	5
Israel	130	120	90	90	4	4
France	130	120	56	56	6	4
England	135	125	84	84*	4	3
Brazil	130	125	60	90	4	3

*84 permitted, 112 recommended

Donor Iron Stores at Enrollment

REDS-II Donor Iron Status Evaluation (RISE) Study, n=2,425

	Median and range, ferritin (ng/ml)	% ferritin < 12 ng/ml
1st time donors		
male	108 (29-430)	0
female	37 (9-175)	6%
frequent donors		
≥3/yr males	25 (6-117)	16%
≥2/yr females	19 (5-68)	27%

Cable, Transfusion, 2011; 51:511.

Iron Stores in Female Donors Failing Initial Fingerstick Hemoglobin Determination

M Goldman, S Uzicanin, V Scalia, SF O'Brien
Canadian Blood Services, Ottawa, Ontario, Canada



Transfusion 2012 (35); 89A

Hb and ferritin status in female donors, according to initial Hb pass or fail

Cohort		# of donors	Hb g/L		Ferritin (µg/L)		
			1 st measurement mean (95% CI)	2 nd measurement mean (95% CI)	<12 # (%)	12-24 # (%)	>25 # (%)
Initial Hb pass	High pass Hb>130 g/L	213	141.0 (140.0- 142.1)	NA	27 (13)	81 (38)	105 (49)
	Low pass Hb 125-129 g/L	60	127.0 (126.7- 127.4)	NA	15 (25)	25 (42)	20 (33)
Initial Hb fail	Second Hb pass	22	119.8 (118.2- 121.4)	133.5 (130.8- 136.2)	13 (59)	7 (32)	2 (9)
	Second Hb fail	47	116.5 (114.6- 118.4)	116.8 (115.0- 118.6)	33 (70)	9 (19)	5 (11)

International developments

- Studies from Denmark, Germany, Iran, Switzerland, and Australia on iron replacement
- In some small blood centres (Swiss Red Cross in Basel, Copenhagen University, NIH) routine ferritin measurement and iron supplementation have resulted in increases in mean Hb, ferritin levels
- Hb level and/or trend may be useful in determining interdonation interval for individual donors

O'Meara, Transfusion 2011; 51:2183

Magnussen, Transfusion 2008; 48:749

Bryan, Transfusion epub Dec 2011

Baart, Transfusion epub 2012

What should we be doing?



"Mr. Osborne, may I be excused? My brain is full."

What should we be doing?

- Situation in each country will vary, depending on
 - donor population – age, gender, nutritional status
 - donor criteria for Hb
 - minimum interdonation interval and actual donation frequency
 - organization and staffing of blood centres
 - link between blood centres and health care system
- Each centre can try and answer a series of questions using their own data, and results of studies performed in similar donor groups

Donor vigilance

- Are we providing donors with enough information about iron?
 - donor survey about diet, supplements, MD discussion
- Are donors who fail their Hb screen being appropriately counselled?
 - return rate, Hb in these donors
- Are our donors/a subset of our donors at high risk for iron deficiency?
 - frequency of donation, Hb levels and deferral rates by donor age group and gender

Donor vigilance

- Would measurement of iron status be useful in all or a subset of our donors?
 - measurement by blood centre or donor's MD
 - what actions would donors take
 - impact on donor return, Hb
- Would iron supplementation be useful or feasible?
 - trial of supplementation
 - impact on donor well-being
- Should we increase the minimum interdonation interval?
 - based on donor gender, age
 - Hb level or trend
 - based on measurement of iron status

Conclusions

- Increasing recognition that iron deficiency is common in donors
- Health impacts incompletely understood
- Risk factors for iron deficiency include donor gender, age, frequency of donation, biological variability
- Donor vigilance can assist blood centres in assessing extent of the problem and possible solutions in their setting