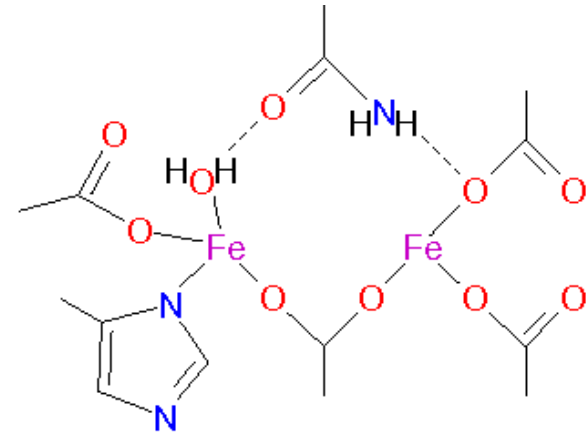
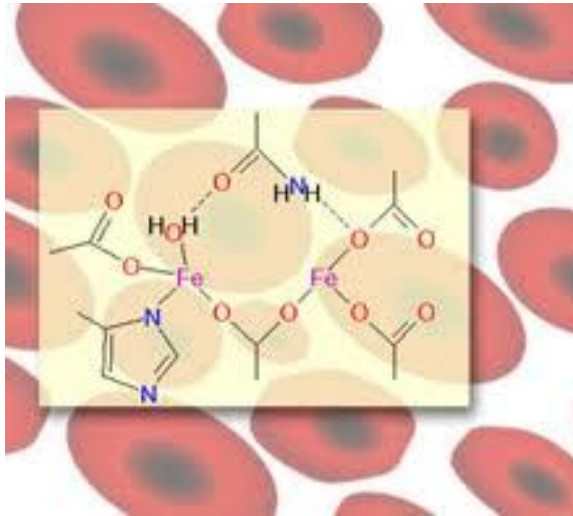


Donor hemoglobin and iron stores



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14th International Hemovigilance Seminar
Montreal, April 25-27, 2012

BACKGROUND

- When collecting blood donations, we remove a certain amount of hemoglobin and iron, which must be replaced.
- In order not to remove hemoglobin from anemic donors, hemoglobin levels are usually measured pre-donation and only donors above a determined threshold are accepted.
- Also, donors are deferred for a defined period of time after RBC donation in order to allow for recovery of hemoglobin mass and iron stores.
- Recently, the criteria used in North America to accomplish these goals have come under closer scrutiny.



DONOR HEMOGLOBIN

- Measuring a donor's hemoglobin and collecting blood only from those with an « acceptable » level :
 - ➔ Avoids the collection of blood from anemic donors
 - ➔ Ensures a sufficient amount of red cells in the final product
 - ➔ Serves as a parameter of general donor health
- Individuals of black race have lower normal hemoglobin levels than caucasians
- Hemoglobin is a poor predictor of iron stores

DONOR HEMOGLOBIN

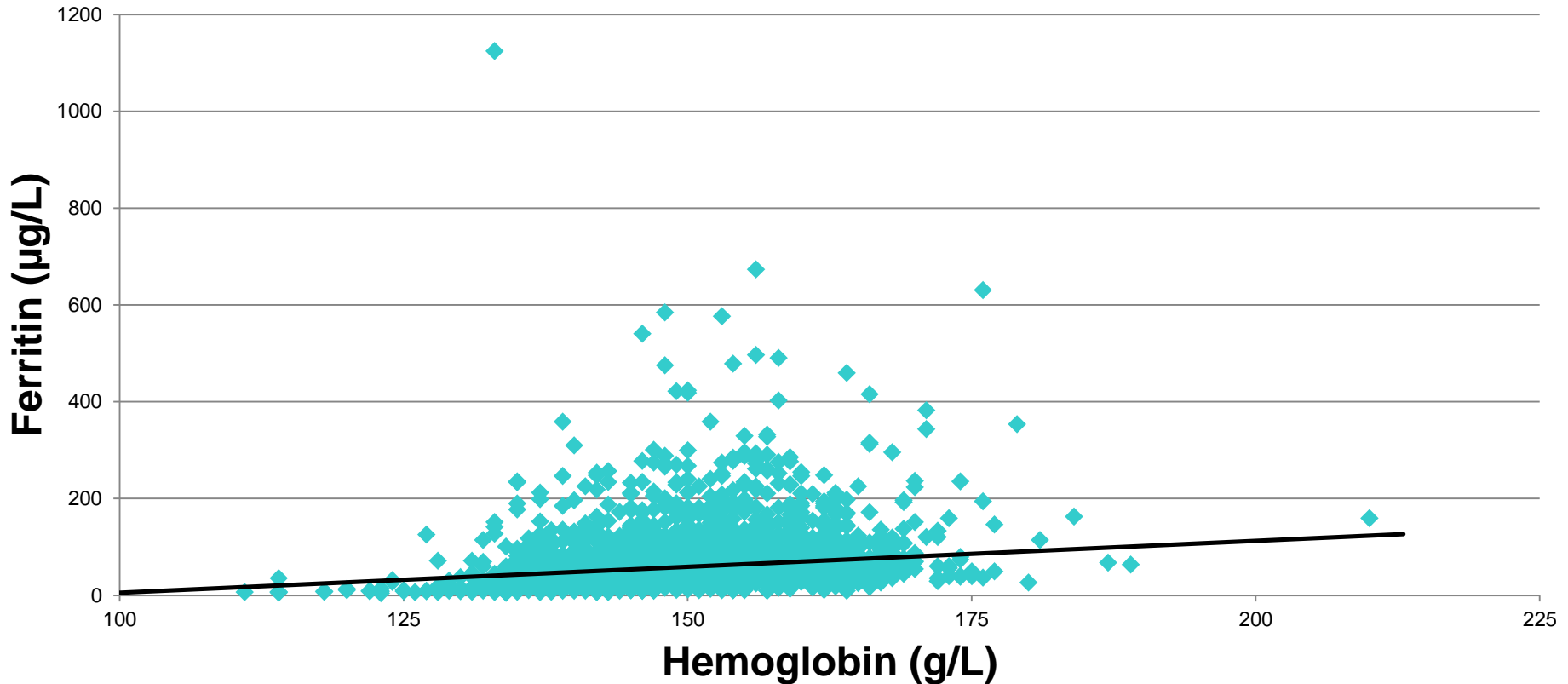
Group	HGB level below which 5% of normal subjects in the population will be found (g/L)
White men 20-59	137
Black men 20-59	129
White women 20-49	122
Black women 20-49	115

NHANES III. Blood 2006; 107: 1747-50



Produits sanguins
Cellules souches
Tissus humains

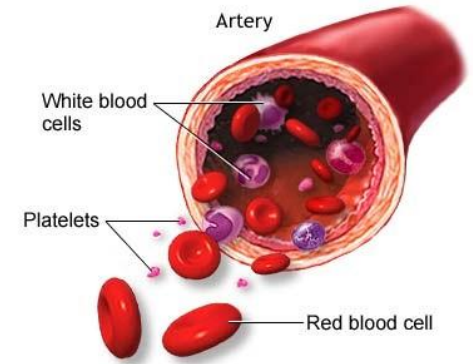
Relationship between ferritin levels and hemoglobin in double red cell donors at Héma-Québec



$r^2=0,116$

IRON STORES

- Ferritin is the best available marker of iron stores
- Iron deletion in blood donors is proportional to the frequency of red cell donation
- Menstruating women are at increased risk of iron depletion following red cell donation



REDS II STUDY*

			ENROLLMENT		FINAL	
	No donations†		AIS	IDE	AIS	IDE
FEMALE	2,6	FT/RA	5%	22%	20%	51%
	4,4	Frequent	27,1%	66%	27%	62%
MALE	2,9	FT/RA	0%	3%	8%	20%
	5,2	Frequent	16%	48,7%	18%	47%

*Cable et al. Transfusion 2012; 52: 702-711

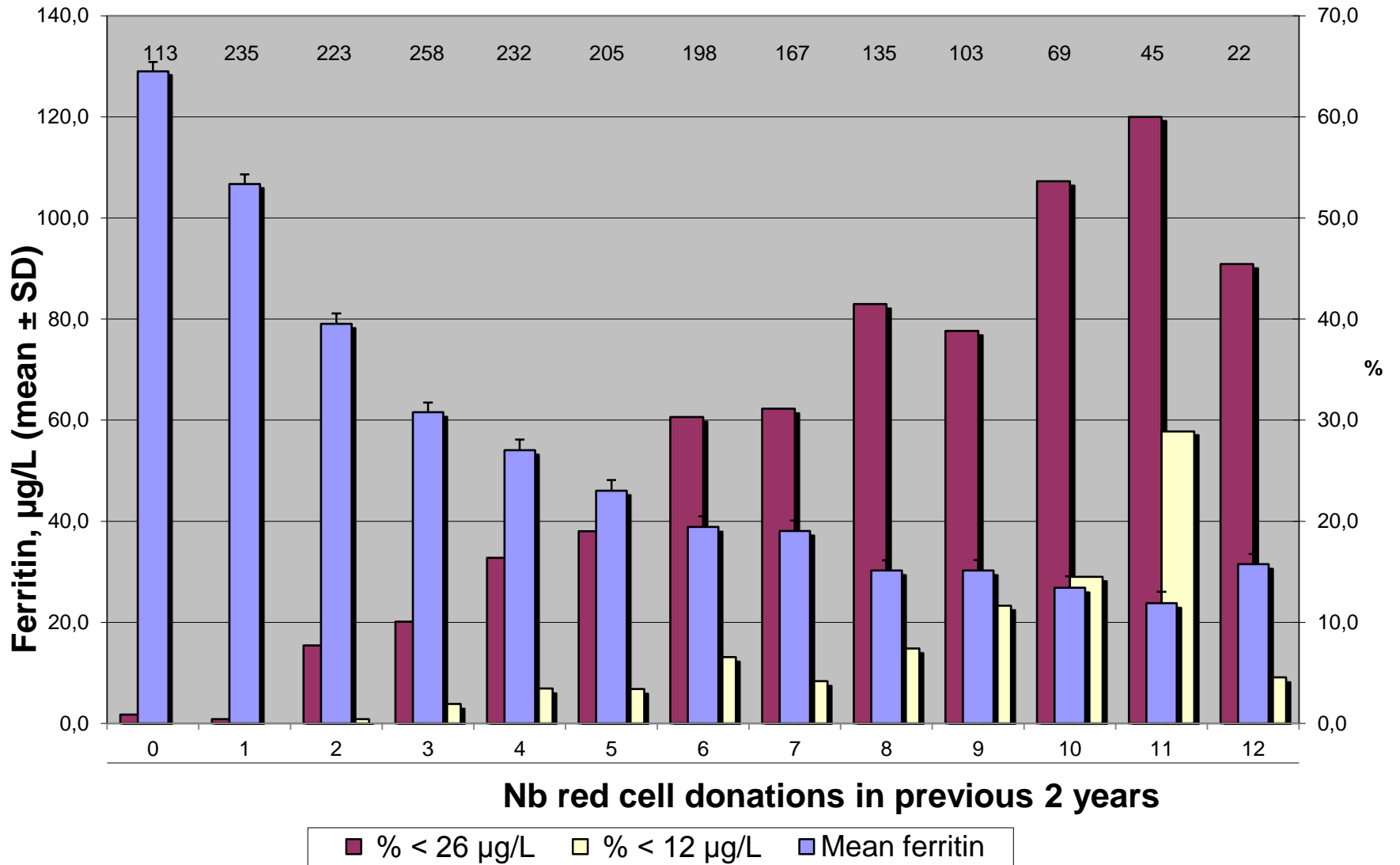
AIS: absent iron stores IDE: iron deficient erythropoiesis

† 2 year follow-up



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Ferritin levels in double red cell donors



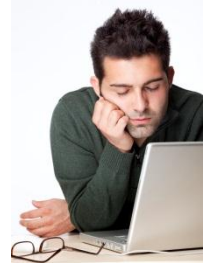
IRON DEPLETION

Impact of iron depletion

- Iron depletion can lead to anemia, which is associated with:
 - Fatigue
 - Reduced work capacity
 - Lack of endurance and limitation of activities
 - Cognitive disorders



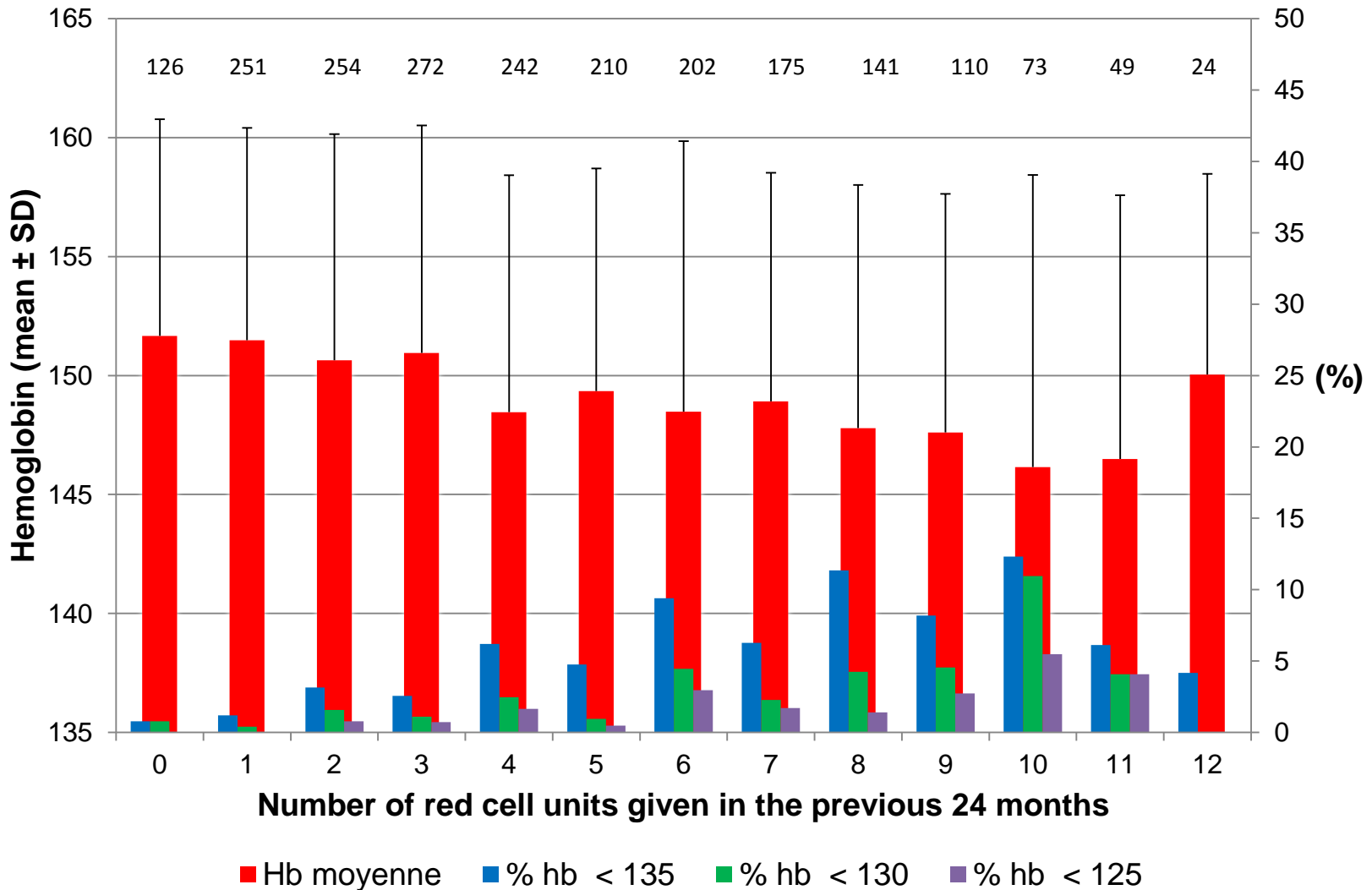
IRON DEPLETION



Impact of iron depletion

- In the absence of anemia, iron depletion can also impede physical and mental functions. These can be corrected by iron replacement. The clinical consequences of iron depletion in blood donors has not been well documented in blood donors.
- Iron depletion is associated with PICA. The association with restless leg syndrome is more controversial.
- Some donors with low iron stores are eventually deferred for a low hemoglobin. Fairly often, these donors undergo fairly onerous medical investigations (including colonoscopies) before it is concluded that their low hemoglobin is due to frequent red cell donations.

DONOR HEMOGLOBIN LEVEL AT LAST VISIT IN DOUBLE RED-CELL DONORS AT HÉMA-QUÉBEC



WHAT CAN BE DONE TO PREVENT AND/OR CORRECT LOW IRON STORES DUE TO RED CELL DONATION?

- Give better information to donors concerning the impact on iron stores of red cell donation
- Give iron replacement
- Monitor ferritin levels
- Increase inter-donation intervals



INFORMATION TO DONORS

- Information pamphlets given to donors should include more detailed information on the effects of red cell donations on iron stores, especially in frequent donors (> 2 RBC donations /year), and menstruating women
- The same information should appear on blood establishment web sites
- The information could also raise the possibility of iron replacement using over-the-counter iron tablets, with a recommendation that donors consult their treating physicians concerning this.

INFORMATION TO DONORS

- A more elaborate information package could be developed for double red cell donors, and menstruating women.
- If a blood donor is referred to his family physician following deferral for low hemoglobin, staff could give the donor information on the number of red cell donations given in the past 2 years. A standard letter to the physician could be given to the donor with that information included.



IRON REPLACEMENT

- A number of studies in the USA and Europe have shown the efficacy of this approach. It raises a number of issues:
 - ➔ Prescription or over-the-counter?
 - ➔ Should ferritin levels be measured before the tablets are given ?
 - ➔ How do we ensure compliance (at best 70%)?
 - ➔ Who pays for the tablets?
 - ➔ Who takes charge of donor follow-up?
 - ➔ Establishment?
 - ➔ Family physician?



IRON REPLACEMENT

- ➡ Safety issues.
 - ➡ Side effects.
 - ➡ Donor hemochromatosis
 - ➡ Inadvertent child poisoning



HÉMA-QUÉBEC

Produits sanguins
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MONITORING FERRITIN LEVELS

- Monitoring of ferritin levels, with iron supplementation of donors with low ferritins is an option
- Such a program was recently implemented successfully in a blood establishment in Switzerland
- Issues :
 - ➔ Costs (2,70 \$ par test at Hema-Quebec)
 - ➔ Who should we test? All? Frequent donors? Menstruating women?
 - ➔ Difficult to implement in mobile drives (need to centrifuge specimen within a short time frame)
 - ➔ Medical follow-up



INCREASE INTER-DONATION INTERVALS

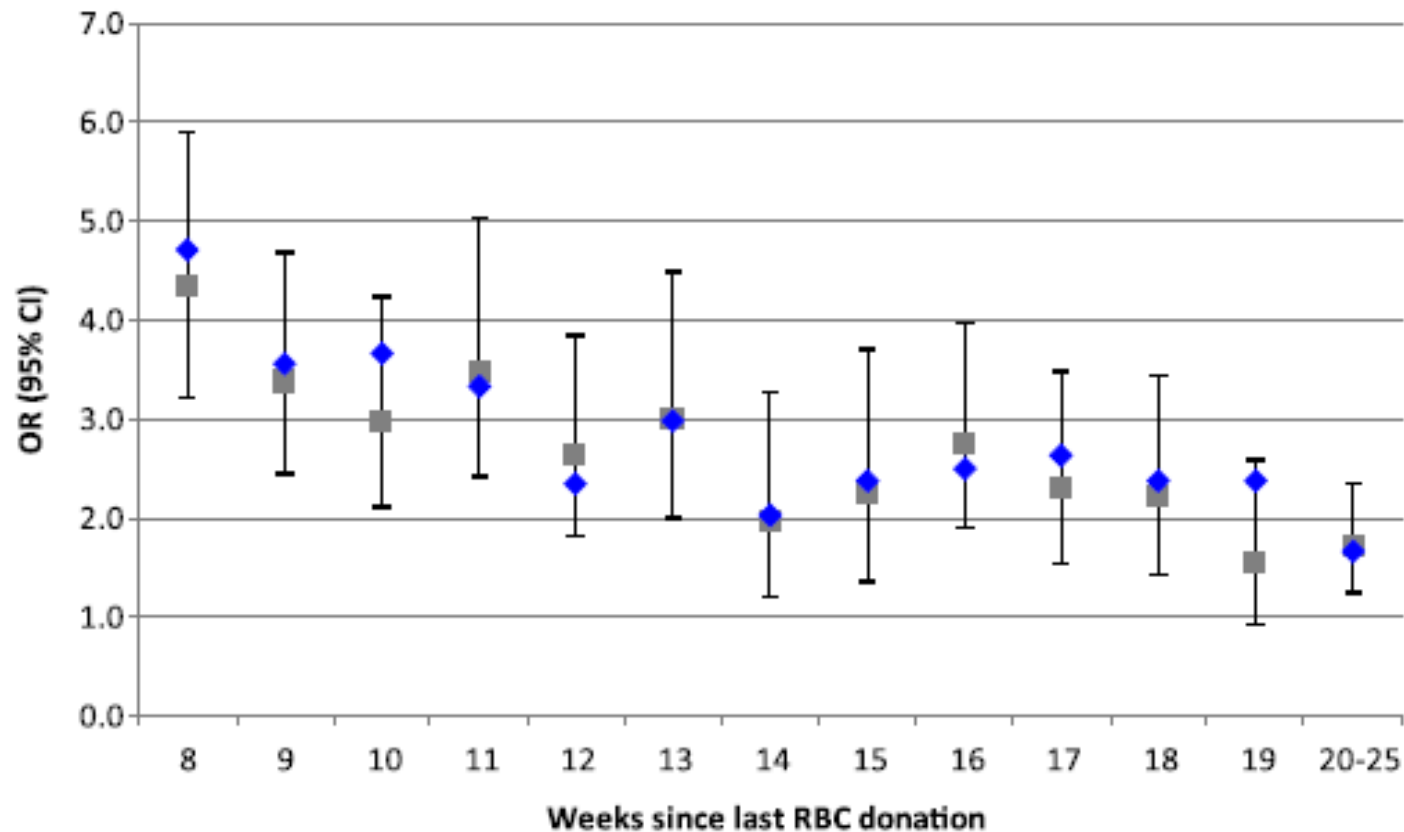
- Advantages:
 - Simple to implement
 - 100% compliance ensured
- What interval to choose?
 - 3 months? 4 months? 6 months?
 - Lengthier in women?
- Major impact on blood supply. Requires the recruitment of replacement donors
- Disproportionate impact on O negative supply



INTER-DONATION INTERVALS

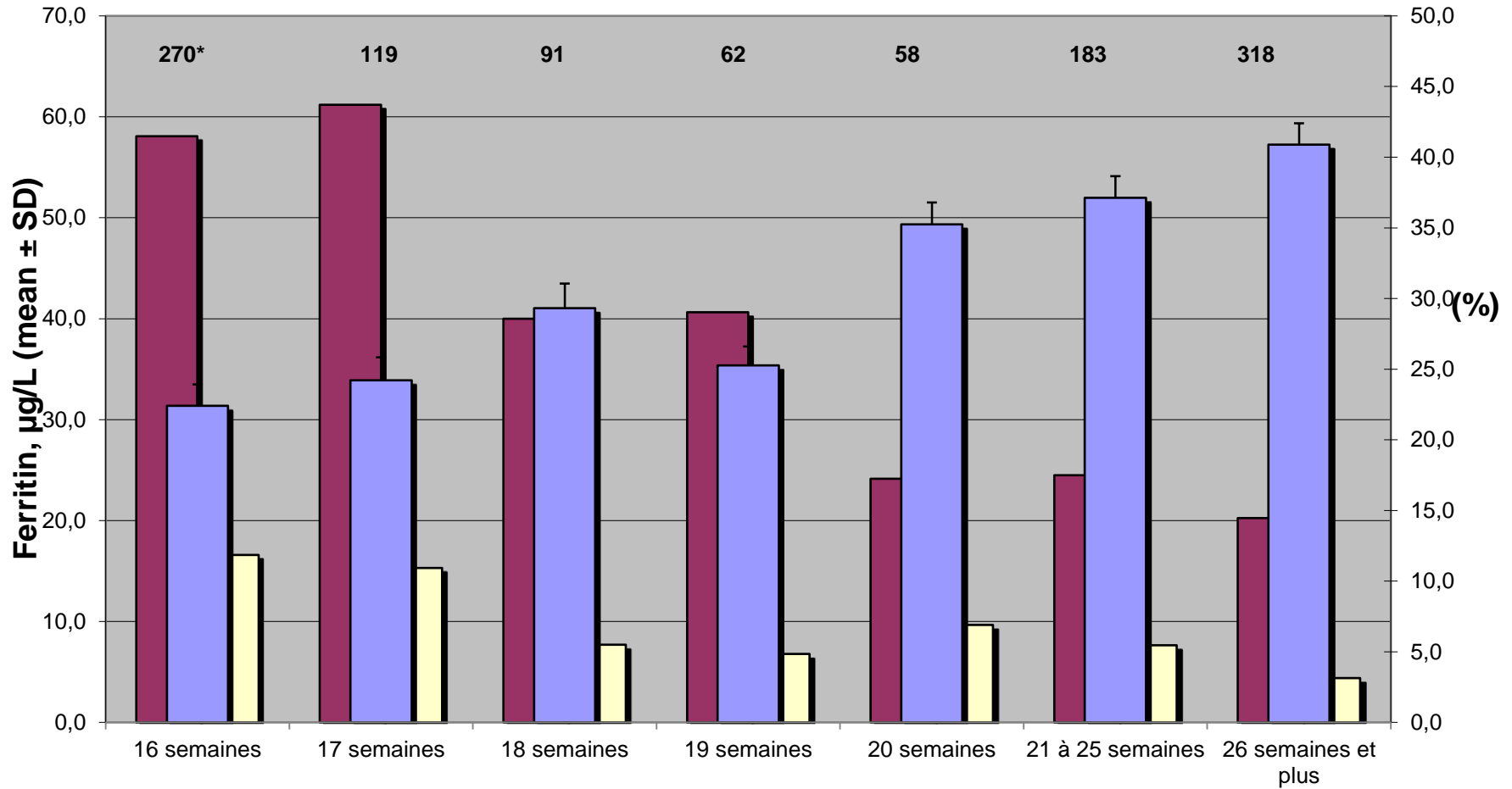
Country	Donation frequency
USA, Canada	56 days
Switzerland	♀, 3x/y ; ♂, 4x/y
France	56 days ; ♀, 3x/y ; ♂, 4x/y
Australia	84 days
Israel	90 days, 4x/y
Council of Europe	56 days ; ♀, 4x/y ; ♂, 6x/y
UK	♀, 3x/y ; ♂, 4x/y (recently)
Scotland	84 days; 3x/y
Germany	56 days ; ♀, 4x/y ; ♂, 6x/y
Sweden	84 days ; ♀, 3x/y ; ♂, 4x/y
Brazil	♀, 90 days, 3x/y ; ♂, 60 days, 4x/y
Hong Kong	♀, 3x/y ; ♂, 4x/y

ADJUSTED ODDS RATIOS (\pm 95% CI) FOR ABSENT IRON STORES OVERALL AND FOR FEMALE DONORS (FREQUENT)



Cable et al. RISE study, Transfusion 2011

FERRITIN LEVELS VS INTERVAL FOLLOWING PREVIOUS DONATION IN DOUBLE RED CELL DONORS AT HÉMA-QUÉBEC



Interval following donation (weeks)

■ % Fer < 26 □ % Fer < 12 ■ Moyenne



Produits sanguins
Cellules souches
Tissus humains

IMPACT OF SCENARIOS ON BLOOD SUPPLY AT HQ

Hgb ♂	Hgb ♀	Donations/y ♂	Donations/y ♀	%
125	125	6	6	100
125	120	6	4	103,2
125	120	6	3	102,4
125	125	4	4	98,5
125	125	3	3	94,8
125	125	2	2	85,6
125	125	6	4	99,8
125	125	4	3	97,8
125	125	4	2	94,9
130	120	4	3	100,1
130	120	6	3	101,4

CONCERNING DONOR HEMOGLOBIN CRITERIA

- In North America, the hemoglobin threshold for blood donation in both men and women is 125g/L. This is related in part to the fact that until recently, donors were tested first by the copper sulfate method.
- This uniform hemoglobin threshold results in the deferral of women with normal hemoglobin levels ($\geq 120\text{g/L}$) and normal iron stores. This threshold also allows the collection of blood from anemic male donors.
- Therefore, it makes “physiological sense” to have a higher threshold in men, and a lower threshold in women.
- Increasing the donor hemoglobin threshold in men could be compensated by a reduction in the threshold for women to 120g/L, even if we limited the number of annual donations in women to 3.
- Should we have lower criteria for individuals of black race?

HEMOGLOBIN CRITERIA

Country	Hgb-males (g/L)	Hgb-female (g/L)
USA, Canada, Switzerland	125	125
France, Australia, Israel	130	120
Council of Europe, UK, Scotland, Germany, Sweden	135	125
Brazil	130	125
Hong Kong	130	115

CONCLUSIONS

- Depletion of iron stores occurs frequently in blood donors, particularly in menstruating women and frequent red cell donors.
- There is no simple straightforward solution to the issue.
- A combination of approaches may be the better solution.
- There is still a great need for clinical research on this issue



QUESTIONS?



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