Sykehuset Innlandet HF

Handling low Haemoglobin and Iron Deficiency in Danish Blood Donors

May 18th 2018, Paris; Société Française de Sanguine

Fer et médecine transfusionelle, patients et donneurs;

Karin Magnussen

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Background - Iron

- Iron is needed in all organisms
- Iron is a prerequisite for life
- In man iron is e.g. needed for
  - Haemoglobin
  - Myoglobin
  - DNA and RNA synthesis
  - ATP generation
  - Brain enzymes
- Too much iron is toxic

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Iron and Blood Donation

- One blood donation 450ml; samples 40ml
- Content of iron is dependent on the Hb concentration
  - Hb 12.5 g/dL contains 215 mg
  - Hb 15.0 g/dL contains 255 mg
  - Hb 18.0 g/dL contains 307 mg
- Ferritin 30µg/l corresponds to 215 mg iron

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Question 1: which statement is wrong?

A) ferritin <15 micrograms/l is a good indicator of iron deficiency

B) iron tablets are best absorbed if taken with at least 24 hours intervals

C) iron deficiency is rare

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How Haemoglobin depends on Iron

- Iron is a prerequisite for haemoglobin to be formed
- With sufficient iron, you have your habitual haemoglobin conc.

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- With sufficient iron, you have your habitual haemoglobin conc.
- With an iron deficient diet, iron is secured from storage (ferritin drops)
- An empty iron storage + iron deficient diet, leads to drop in haemoglobin
- With an increased iron intake, the haemoglobin conc. will increase
- With continued increase in iron intake, ferritin will increase

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Low Haemoglobin and iron deficiency; a global challenge

- In 2010 16 % of our donors had ferritin< 15µg/L

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Consequences of iron deficiency

- No Iron stores for pregnancy
  - May lead to pre term birth an small for date
- Anaemia
- Muscle fatigue and reduced endurance
- Impaired cognitive functions
- Clinical symptoms
  - Pica
  - Restless legs syndrome
  - Nail and mouth problems

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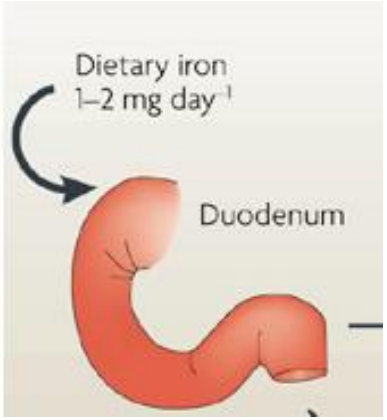
Iron; Uptake and Storage



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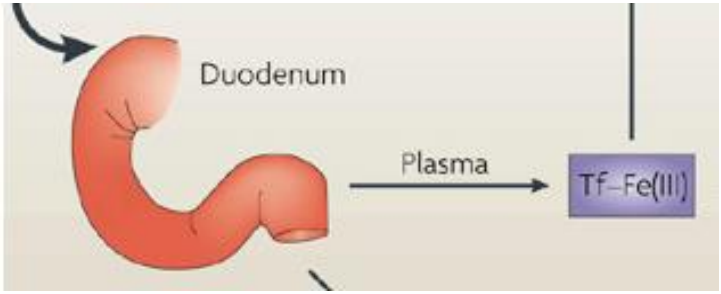
Iron; Uptake and Storage



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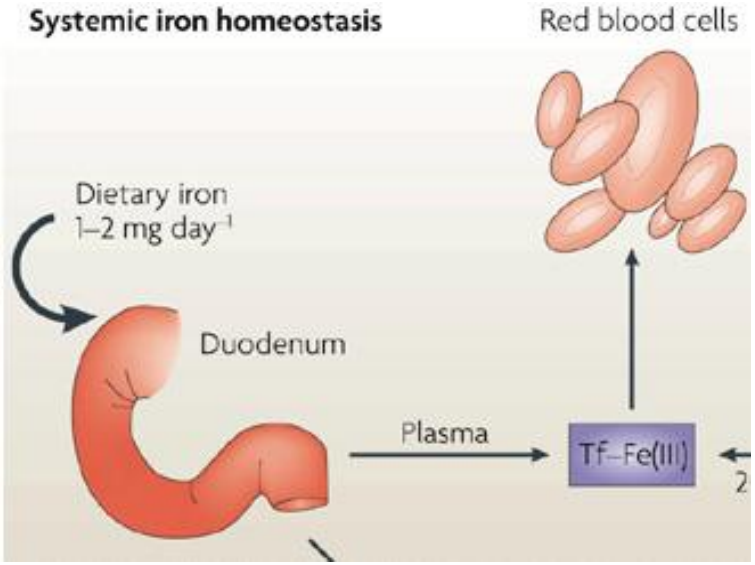

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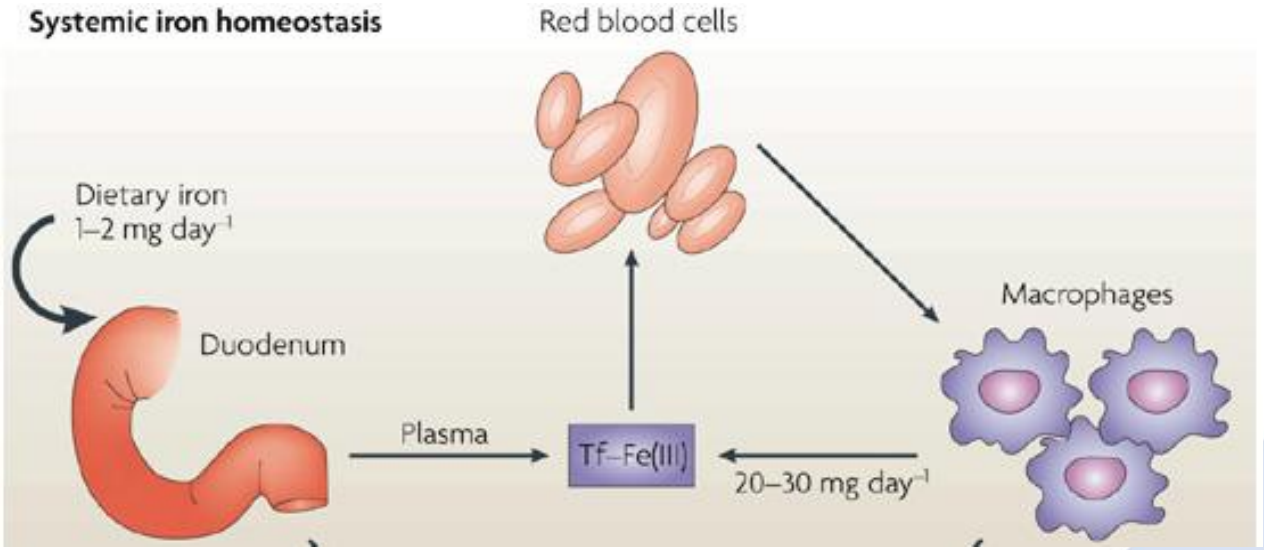

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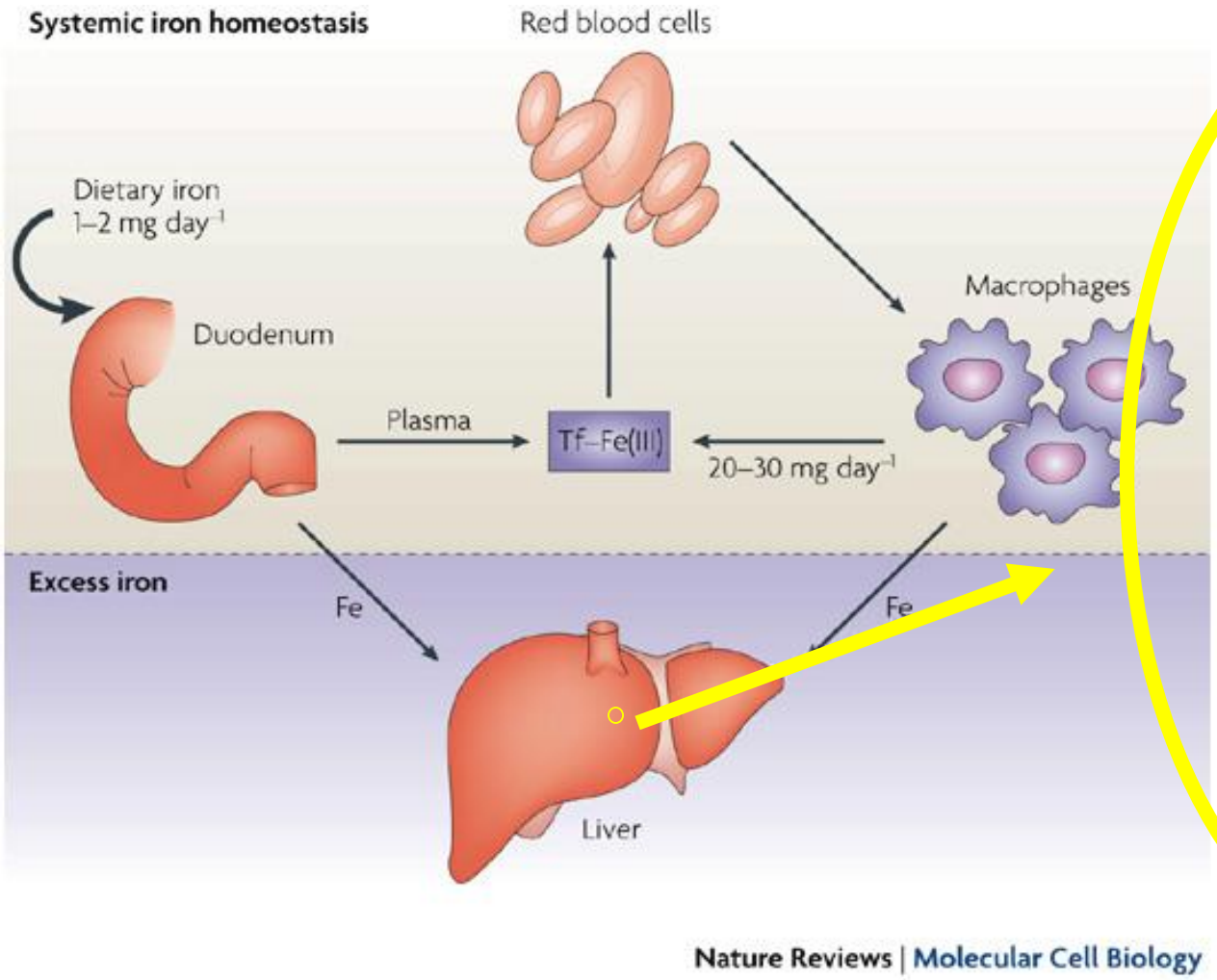

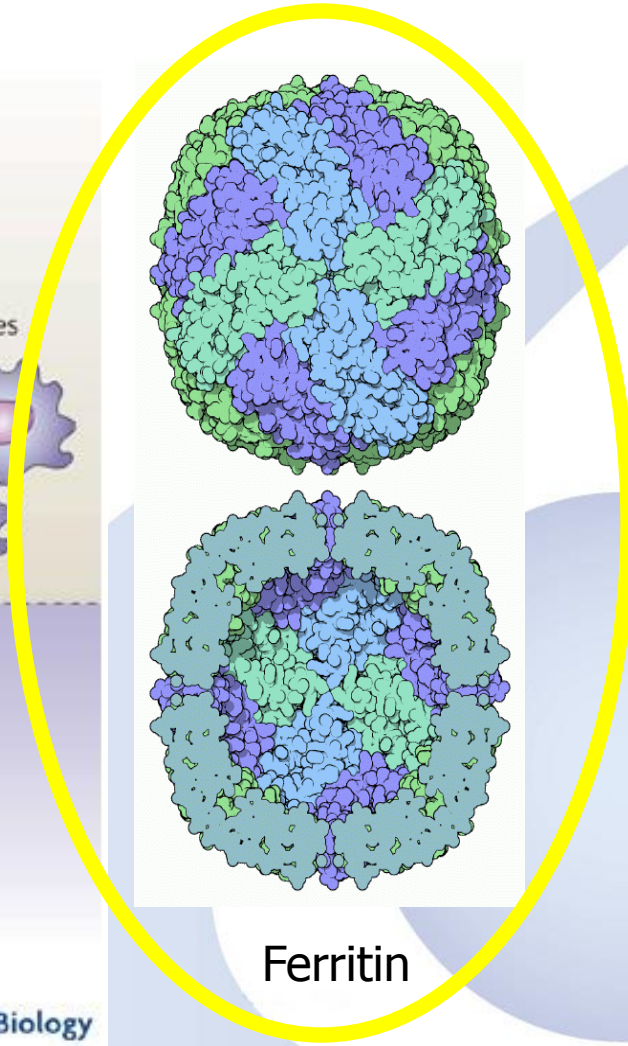

Ferritin

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Question 2: is iron best absorbed in a basic environment?

- Yes

- No

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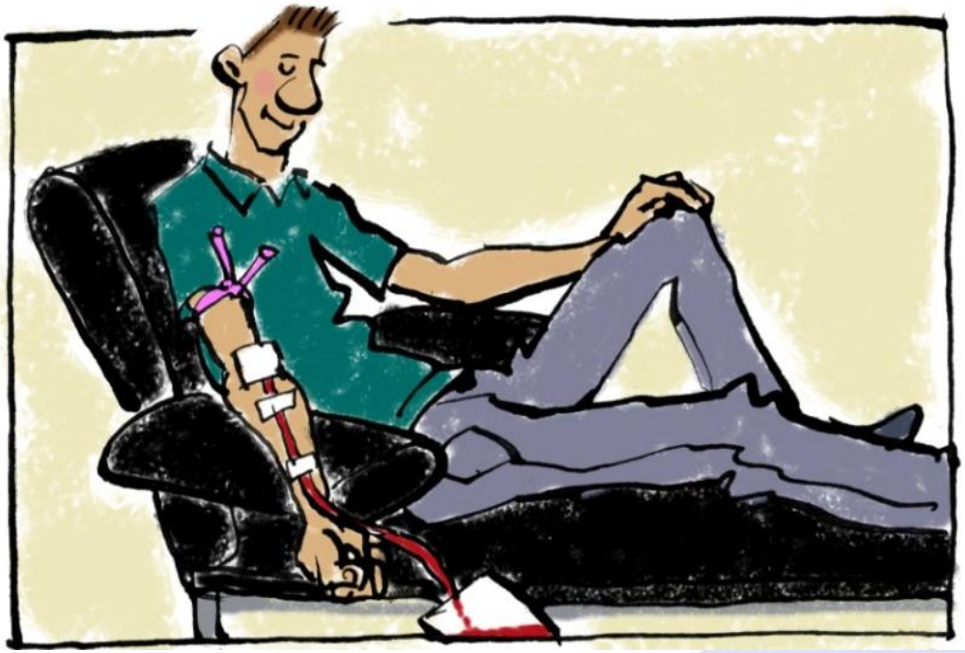
The first time donor



25% of female first time donors have low ferritin <30µg/L

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Regeneration after Donation

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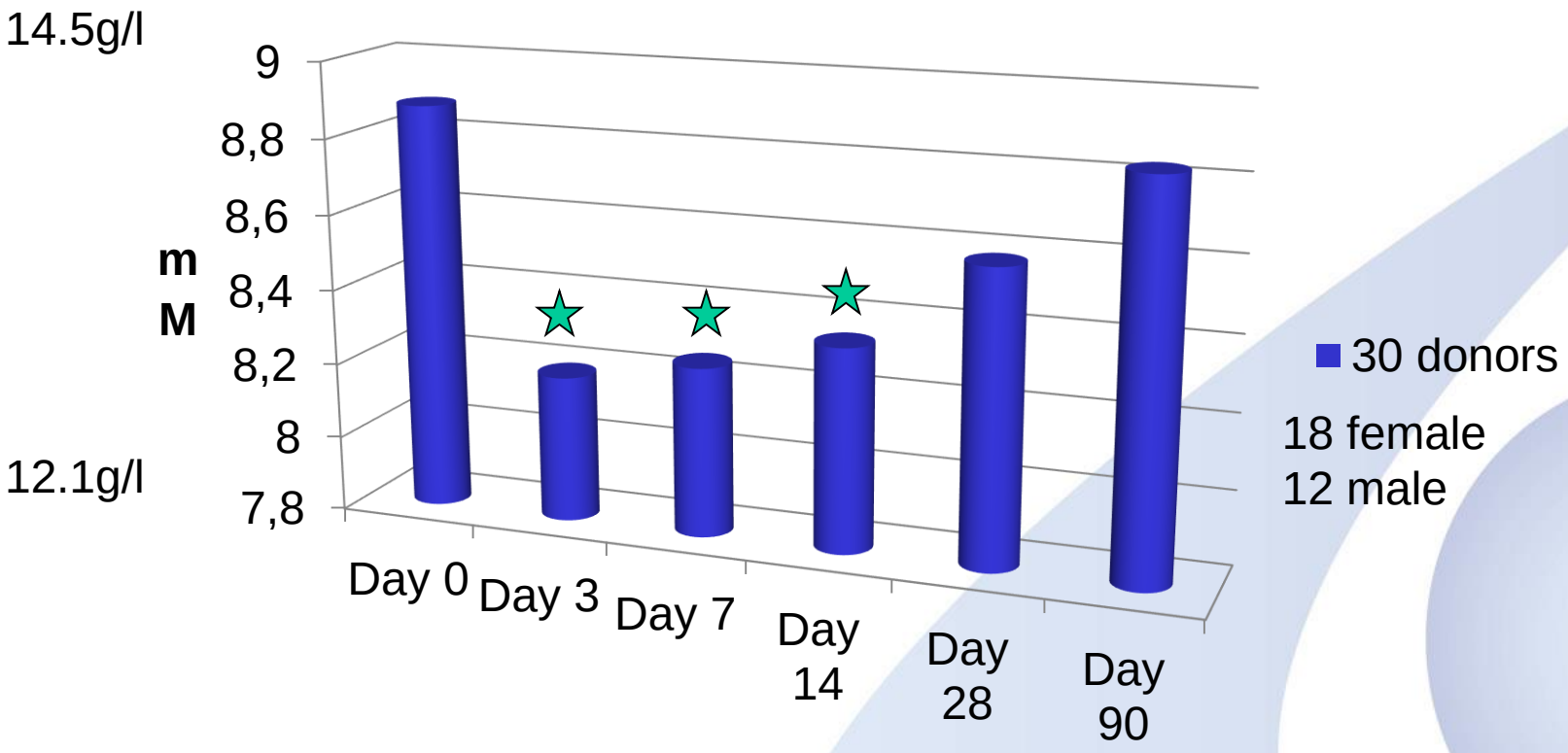
Regeneration of Hb post donation

in non- iron deficient donors



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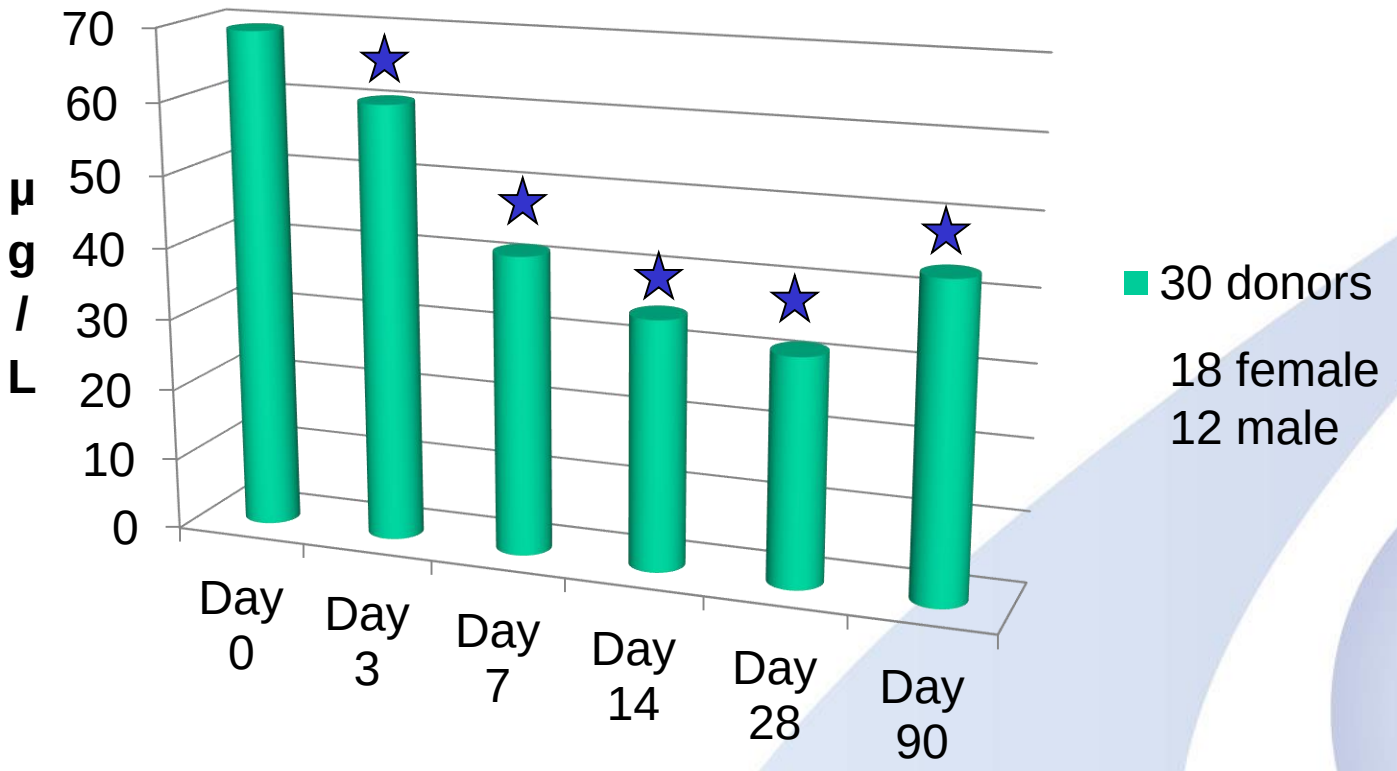
Regeneration of Ferritin post donation

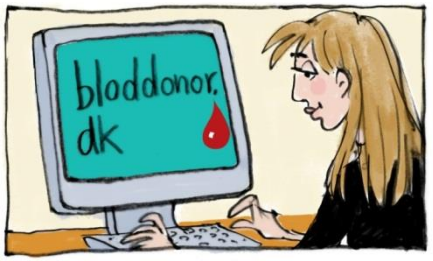
in non- iron deficient donors



The Program implemented in Copenhagen

Emphasis on making it simple

- Ferritin measurements
- Hb and ferritin measurements were centralized
- A resource team takes care of all questions related to Hb and ferritin *(specially trained Biotechnicians)*
- The Hb samples are taken before donation, and carried to Centre for Donor Haemoglobin and Iron where it is analysed on Sysmex (XE-2100D)
- Ferritin is measured on the sample also used for viral markers
  - All donors and every 10th donation and since Aug 2013 a control Ferritin was taken on donors with low Hb or F



Algorithm

For any donor presenting at the blood center

F: Hb ≥ 12.5 g/dL
M: Hb ≥ 13.5 g/dL
and
Ferritin ≥ 60 or not done

No action
F: n=96,285
M: n=132,769

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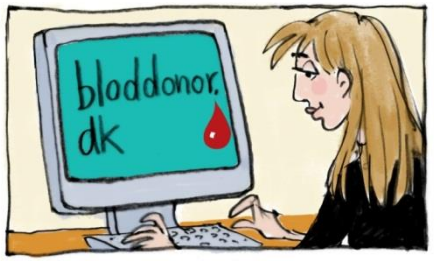

Algorithm

For any donor presenting at the blood center

F: Hb ≥ 12.5 g/dL
M: Hb ≥ 13.5 g/dL
and
Ferritin < 60

Ferritin 30-60
F: n=18,615
M: n=9,423

20 iron tablets at future donations

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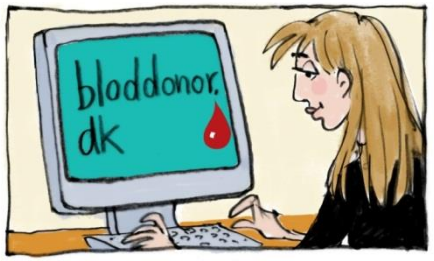


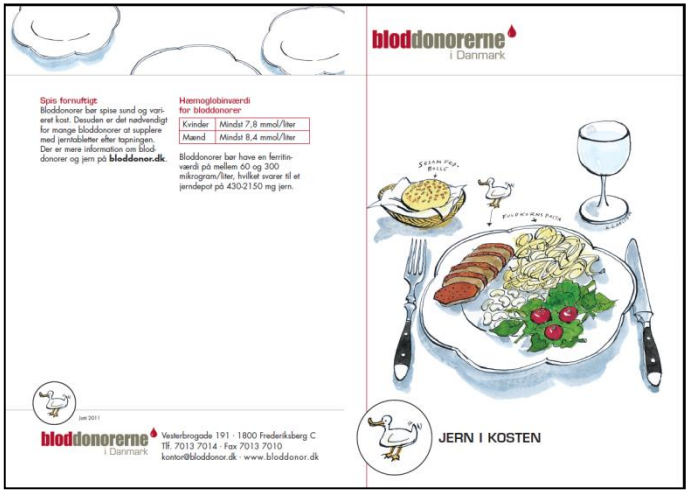
Algorithm

For any donor presenting at the blood center

F: Hb ≥ 12.5 g/dL
M: Hb ≥ 13.5 g/dL
and
Ferritin < 60

Ferritin ≤ 30
F: n=15,519
M: n=3,009

60 iron tablets and iron leaflet by post
and
20 iron tablets at future donations



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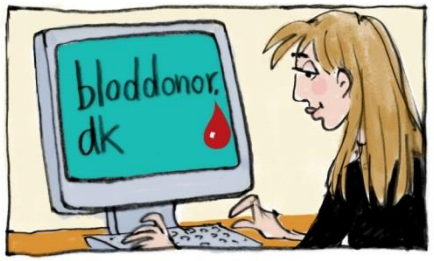


Algorithm

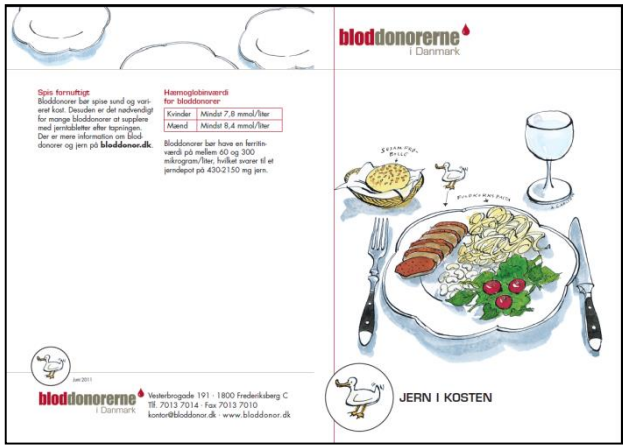
For any donor presenting at the blood center

F: Hb < 12.5 g/dL
M: Hb < 13.5 g/dL

Phone call:
History from and information to the donor

Ferritin 15-40
F: n=965
M: n=74

60 iron tablets and iron leaflet by post and
20 iron tablets at future donations.
Or if suspect history GP



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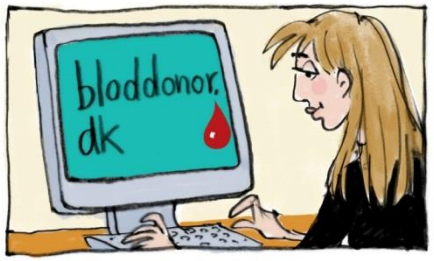


Algorithm

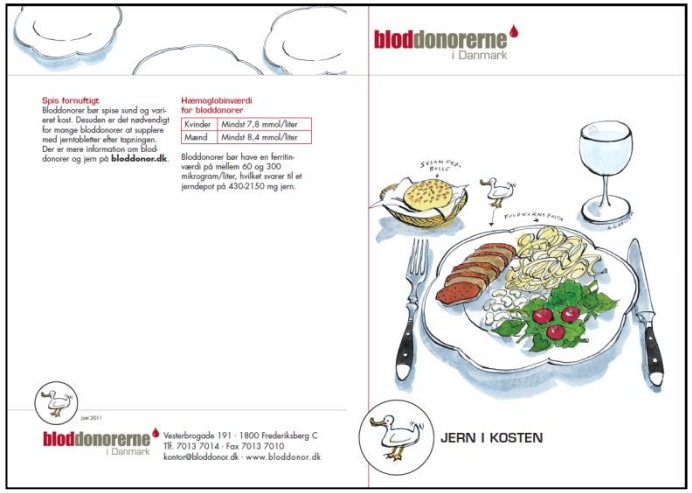
For any donor presenting at the blood center

F: Hb < 12.5 g/dL
M: Hb < 13.5 g/dL

Phone call:
History from and information to the donor

Ferritin ≤ 15
F: n=1,043
M: n=64

100 iron tablets and iron leaflet by post and 20 iron tablets at future donations.
Or if suspect history GP



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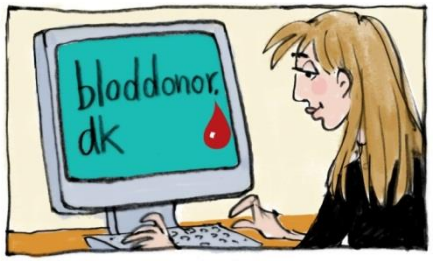

Algorithm

For any donor presenting at the blood center

F: Hb < 12.5 g/dL
M: Hb < 13.5 g/dL

Phone call:
History from and information to the donor

Ferritin ≥ 40 or not done
F: n=600
M: n=291

GP

Iron tablets

JernC
Ferrous fumerate 100mg + Vit C

Price/20 tablets:
1.15€

AminoJern
Ferrous bisglycinate 25mg

Price/20 tablets:
1.21€

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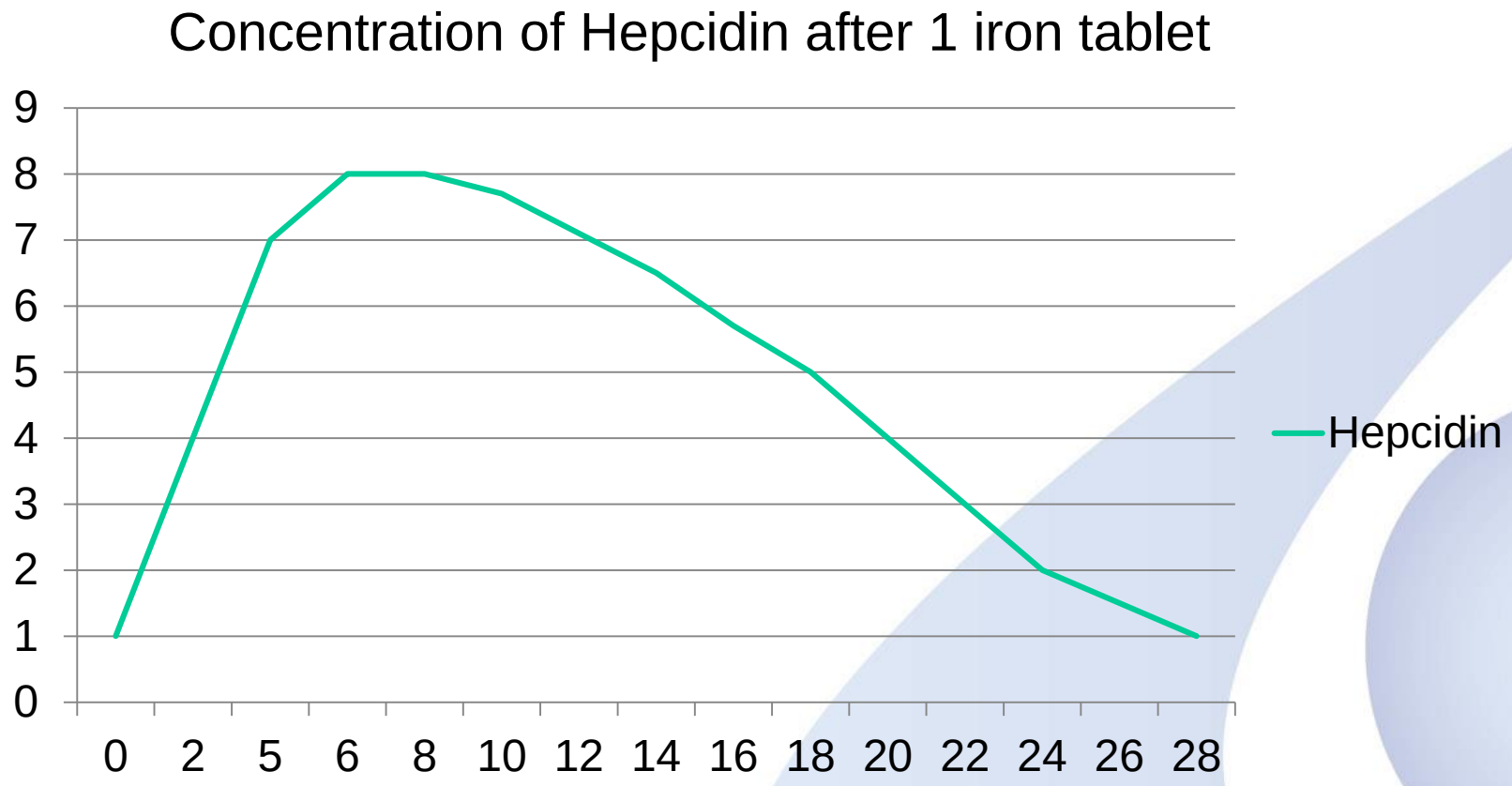
Iron uptake is very difficult to predict, but the main factor is hepcidin



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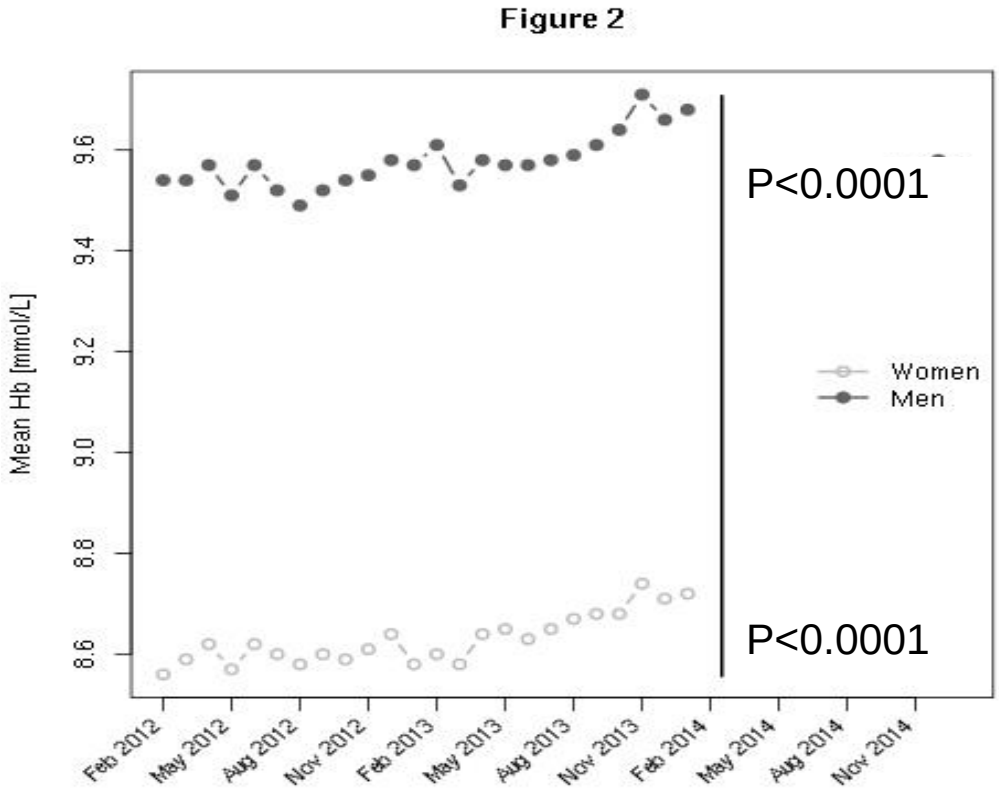
Mean Hemoglobin by Sex and Month

15.5 g/dL

13.9 g/dL



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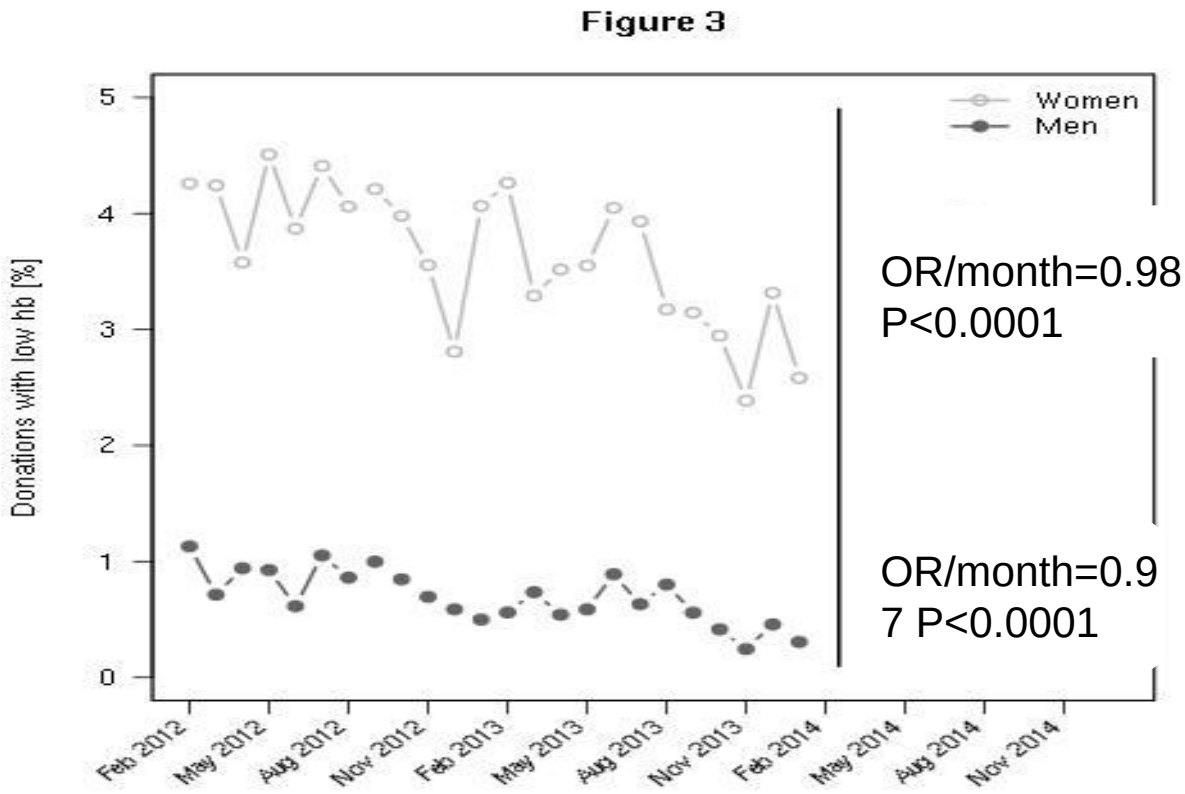
Fraction of Donors with Low Hb



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Question 3: in blood female donors a haemoglobin lower than 12.5 g/dL is often caused by iron deficiency, but may also be caused by disease.

- Yes
- No

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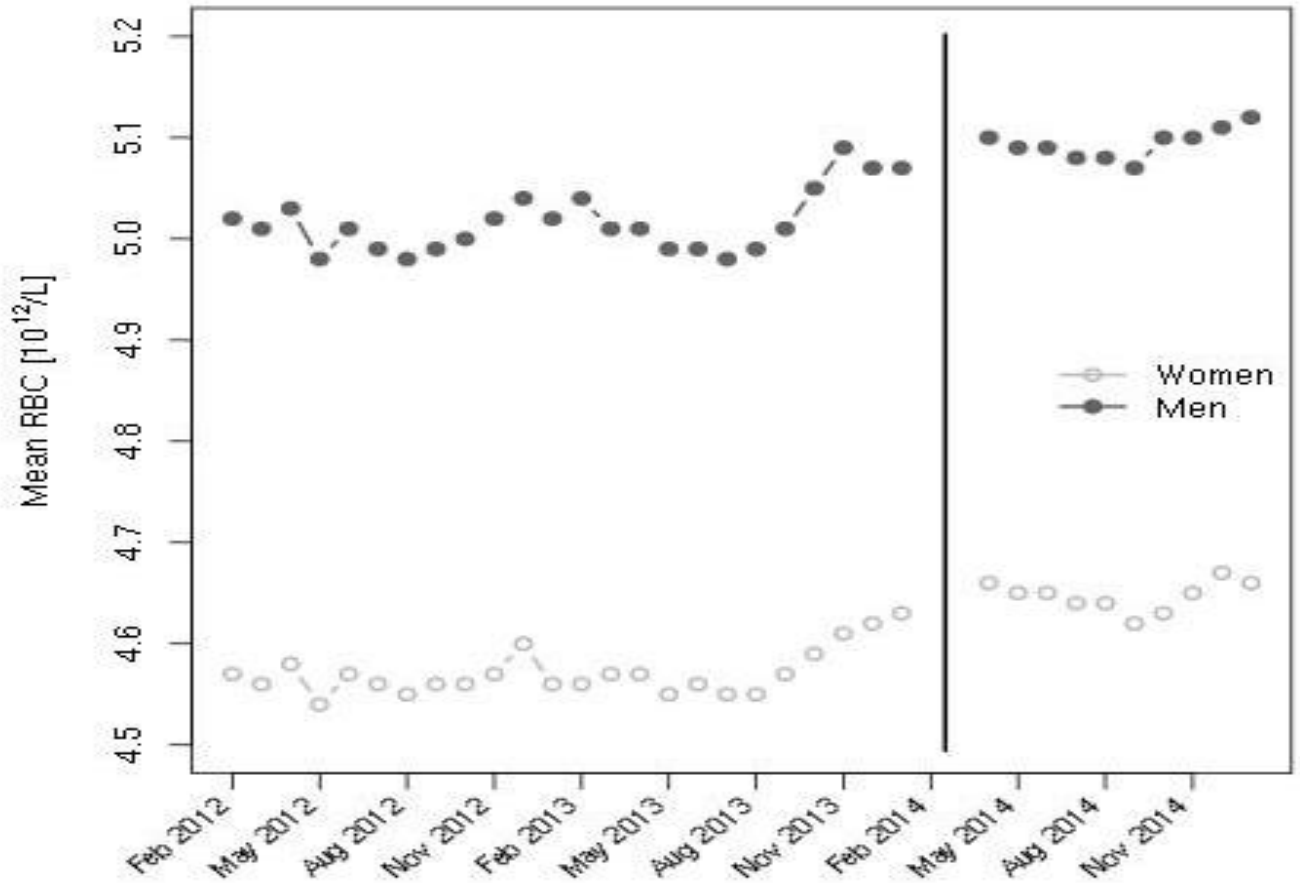
Red Blood Cell Count



P<0.001

P<0.001

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Low Haemoglobin and iron deficiency; a global challenge

- In 2010 16 % of our donors had ferritin< 15µg/L
- In 2016 the number of donors with ferritin < 15µg/L was reduced to 1,9 %

Haemochromatosis

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative								
1 mutation								
2 mutations								
3 mutations								
4 mutations								
Total								

Ferroportin 1 gene (SLC40A1)

Haemochromatosis

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17						
2 mutations	18	36						
3 mutations	4	12						
4 mutations	1	4						
Total	**49**	**69**						

Haemochromatosis

Sykehuset Innlandet HF

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17	4					
2 mutations	18	36	22					
3 mutations	4	12	4					
4 mutations	1	4	2					
Total	**49**	**69**	**32**					

Haemochromatosis

Sykehuset Innlandet HF

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17		8				
2 mutations	18	36		10	1			
3 mutations	4	12		3				
4 mutations	1	4						
Total	**49**	**69**		**21**	**1**			

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Haemochromatosis

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49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17				1		
2 mutations	18	36					1	
3 mutations	4	12					1	
4 mutations	1	4				1		
Total	**49**	**69**				**2**	**2**	

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Haemochromatosis

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17						4
2 mutations	18	36						2
3 mutations	4	12						4
4 mutations	1	4						1
Total	**49**	**69**						**11**

Haemochromatosis

49 donors Ferritin>500µg/l	No. donors	No. mutations	C282Y	H63D	S65C	HFE2	HAMP	TFR2
Negative	9	0						
1 mutation	17	17	4	8		1		4
2 mutations	18	36	22	10	1		1	2
3 mutations	4	12	4	3			1	4
4 mutations	1	4	2			1		1
Total	**49**	**69**	**32**	**21**	**1**	**2**	**2**	**11**

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Hemochromatosis

- >300 donors with ferritin > 300 - 400 have been analysed for hemochromatosis mutations
- >80 found with classical hemochromatosis mutations
  - Theoretically we have app. 950 mutation positive donors (HFE 282/282 or 282/63) (0.31+1.42=1.7%)
- Most are heterozygous or have other mutations
- Some are healthy and negative for known mutations
  - And only very few have previously unrecognised inflammatory disease

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Also diagnosed

- 4 Chronic lymphatic leukaemia
- 2 Chronic myeloid leukaemia
- 1 Hairy cell leukaemia
- 1 Multiple Myeloma
- 4 Cancer coli, testis or bladder
- 1 Systemic Lupus
- 2 vitamin B12 deficiency
- Ca 40 Heterozygous α-or β-thalassemia, HbS, E or D
- 1 Polycythaemia Vera
  - 5 in all since 2009

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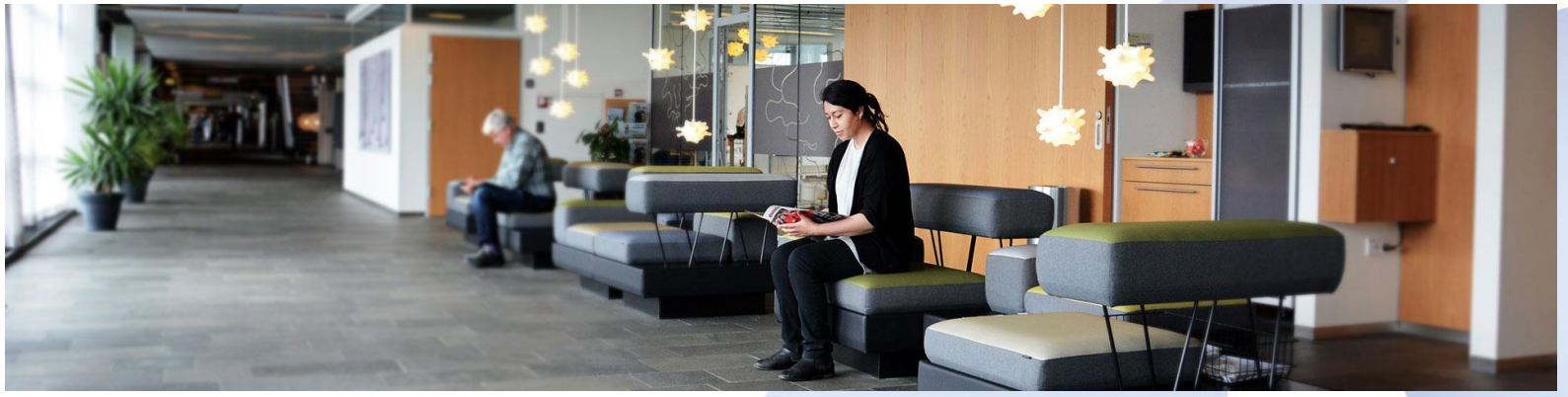
Conclusion

- ✓ An algorithm based on hemoglobin and ferritin
- ✓ Graded iron supplementation restricted to only those that would benefit
- ✓ Resulted in increase in hemoglobin and reduction the number of donors with low hemoglobin
- ✓ Reduction in donors with ferritin < 15 µg/L from 16% to 1.9%



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Merci Beaucoup

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