

JPAC workshop on management of haemoglobin and iron in blood donors

Tuesday 10th June 2008
Grenville Suite, Strand Palace Hotel, 372 Strand, LONDON, WC2R 0JJ

REPORT

The present guideline *UKBTS DSG WB&C Edition 202 Release 09*

The haemoglobin concentration should be estimated each time a potential donor presents. Fingerprick samples should only be estimated with copper sulphate set gravimetrically to determine lower limits of haemoglobin concentration.
Must not donate if the haemoglobin concentration is less than: Female donors: 125 g/l. Male donors: 135 g/l.

Potential donors whose haemoglobin concentration is estimated to be below the acceptable level when tested by copper sulphate should be asked to give a venous sample of blood for further testing. If the venous haemoglobin concentration tested by a validated method is not less than the levels shown above accept.

Introduction

The purpose of this workshop was to identify the important issues and questions that UKBTS needs to tackle with the intention of developing and assessing better approaches to the good clinical care of blood donors (a) to ensure that they are protected against any risks due to anaemia or iron depletion and (b) to minimise the risk of refusing to accept donations from healthy volunteers whose haematological indices are normal for them.

In preparation for the meeting, participants were supplied with some key papers and asked to comment on the following questions to be addressed by the workshop

- Should donor selection be based on haemoglobin levels alone or on haemoglobin plus a measure of iron status?
- Should donor acceptance levels of haemoglobin be based on population norms?
- How should population norms for donor acceptance be established?
- Are current rules for red cell donation frequency correct or should they be modified?
- Are there safe and effective haematinic regimes that enable more frequent donation?
- Are there practicable ways to improve the accuracy and reliability of donor Hb assessment?
- What evidence exists for long term beneficial or harmful effects of donation?

- Is information about ethnicity routinely recorded? If not should it be recorded to enable analysis of haematological data?

Invited speakers were each asked to address a small number of specific questions related to the above. Their full presentations are attached (with permission) as Appendix 1

Key points from the presentations

Professor Martin Pippard

What is meant by normal haemoglobin concentration in healthy individuals?

Anaemia: the haemoglobin concentration below that which represents the steady state for a healthy individual. Population data can indicate the probability of an individual member of that population being anaemic at any given haemoglobin concentration. This normal variation (Gaussian distribution) of haemoglobin concentration reflects individual variations in the physiological mechanisms that control Hb concentration.

Measurement of haemoglobin concentration: Observed values are influenced by (a) physiological factors e.g. capillary or venous, diurnal effects, position and also by methodological factors such as sample site, assay method etc.

What are the effects of reduction in body iron and how may iron status be assessed?

Studies to demonstrate any effect of isolated iron depletion in humans are technically difficult because of need to demonstrate tissue iron depletion and effects of iron repletion. There is little convincing evidence that iron depletion in the absence of lowered Hb concentration is associated with impairment of fatigue, work performance or mental performance. Animal studies indicate that isolated iron deficiency in the absence of anaemia can impair muscle oxidative capacity.

What factors determine the ability of an individual to regenerate red cells following blood donation?

Iron intake from diet and supplements, individual variations in regulation of iron absorption, physiological (and disease related) iron losses, thalassaemia trait

Practical donor management questions:

The essential assessment of an Hb concentration in an individual is: is this Hb level healthy or is it too low for that person?

What would determine if the use of a Hb threshold in the lower part of the normal distribution could risk harm to a donor?

For a person whose Hb is in this range it is essential to establish the cause of the anaemia. For example if it is due to thalassaemia trait there would be no pathophysiological reason to defer, as reflected in the current Donor Selection Guidelines. Other possible causes include malignant disease and peptic ulcer. Consideration must be given to the need for a strategy for investigation and management to avoid possible harm due to delayed diagnosis.

The donor's red cell indices at the time of each donation \pm iron status at the time of donation could help to predict the interval required for Hb level to recover before the next donation and or indicate the need to prescribe iron supplements.

From UKBTS DSG WB&C Edition 202 Release 09

Must not donate if:

Has a sickle-cell or thalassaemia syndrome.

Donors with traits for abnormal haemoglobin: **accept**.

Donors with thalassaemia trait **accept but** advise they may fail the haemoglobin screening test

Dr Frank E Boulton

Should donor selection be based on Haemoglobin concentrations alone or include some measure of iron status?

UK population data on the Hb levels and ferritin levels for men and women of different ages are available from the 1991 Health Survey (ONS) and also from the 2003 Scottish Health Survey. The range is slightly higher in smokers and those with BMI >25, but not affected by reported alcohol consumption or level of physical activity. Data are also available from the MRC Southampton Women’s Study (of preconceptional women).

From the distribution curve of Hb values in this study, the use of a Haemoglobin donation threshold of 120 g/l would exclude 17% of apparently healthy women from blood donation, and a threshold of 125 g/l would exclude 35%.

Single measurements of levels of serum ferritin and soluble transferrin receptor (STr) in populations of donors who have given 1 up to 7 donations show the expected fall in ferritin and rise in soluble transferrin receptor. However these ‘snapshot’ values do not necessarily reflect the changes that may be observed in serial studies on an individual over the course of repeated donations (considered below in Dr Gillon’s presentation).

A possible alternative to the use of iron measurements would be a “Combined Cell Index” i.e. Red cell distribution width RDW ? [MCV x MCH]. This may merit evaluation as evidence presented indicated a correlation with ferritin levels. Another candidate alternative to ferritin or STr may be indices of reticulocyte Hb provided by modern haematology analysers.

Dr Jean Harrison

What special considerations apply to plateletpheresis donors?

At each platelet pheresis the donor loses about 100 ml of whole blood due to sampling and harness deadspace. Study of ferritin levels in 206 male plateletpheresis donors (with no identified pre existing reason for blood loss) showed mean serum ferritin: 48 ng/ml (range 8-485): 37% were below 30ng/ml. As shown below there was a relationship with the frequency of donation, but there was no relationship with the lifetime number of platelet donations (for 10-50 donations, 37% of donors had ferritin levels<30ng/ml, for 51-100 donations, 40% and for more than 100 donations, 36%).

<i>Donation frequency</i>	<i>Males tested</i>	<i>Ferritin <30ng/ml</i>
2 weekly	49	31 (63.3%)
3 weekly	56	26 (46.4%)

4 weekly	71	16 (22.5%)
5/6 weekly	30	4 (13.3%)

Annual ferritin testing of selected donors might enable more frequent donation for some. Blood losses with plateletpheresis could be reduced by changes to sampling regime and design of the collection harness.

Dr Jack Gillon

How useful is the determination of Hb before each donation?

Haemoglobin levels had been recorded over the course of 2- 5 whole blood donations over an 18-month period. The subjects were 392 female donors with haemoglobin levels of 120 – 124 g/l at first attendance. There was data on 655 attendances over the 18 months resulting in 468 donations. Donors gave an average of 1.5 donations/donor/year. In most donors, the predonation Hb levels were maintained.

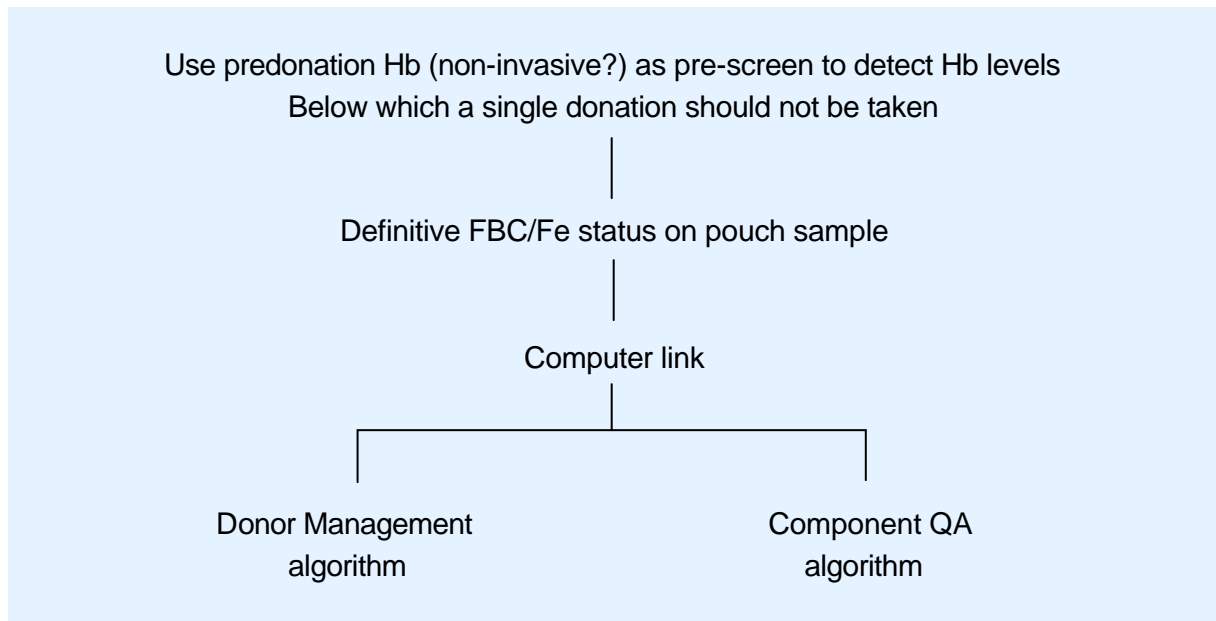
Subsequent attendances and Hb failure rate (Hb <120 g/l)

Attendance	2	3	4	5
Number Attending	330	217	100	15
Hb <120 g/l (%)	92(27%)	51 (24%)	16 (15%)	2 (13%)
Mean Hb	133	124	125	126

No clear relationship was apparent between the rate of deferral for low Hb (<120 g/l) and the interval between donations when the donors attended to give their second and third donations. However, donors giving 2-4 donations may be self-selecting, as non-returning donors may have been those adversely affected by the earlier donations.

The predonation determination of hemoglobin as currently practised by UKBTS is invasive, inaccurate, poorly controlled, unpopular with donors, labour intensive and expensive. It has some value in detection of anaemia before a donation is accepted. However where donation frequency is in the region of 1.5 times per year, the current Hb screen has little value as a predictor of anaemia or iron depletion, as a screen for subclinical disease, or as a predictor of adverse donor events.

One suggestion for a more rational approach to the haematological assessment of donors is illustrated.



Dr Karen Bailie

Haematological data on donors in Northern Ireland. Summary of the data and requirements for data extraction to permit full analysis

Since 2005, the NIBTS Hb screen procedure has been to test donors with an initial copper sulphate test on a finger prick sample, followed by a Hemocue test on a venous sample for those who fail the copper sulphate test. In addition, a venous sample is obtained at each donation (by venepuncture if donor fails Hb screen procedure and from sampling pouch if donor passes the Hb screen procedure). The venous samples are processed the day after donation and Full Blood Count analysis performed on a dedicated Sysmex XT-2000i Analyser.

The FBC data are downloaded and held in Excel spreadsheet format. Data are available for the years 2005 – to present and collection continues, for approximately 60,000 donors per year (10% first time). The data to be extracted for analysis consists of:

By donor number: Gender, age, donation history, deferrals.

By donation number: Haematological parameters i.e. Hb, RCC, PCV, MCV, MCH, MCHC, RDW WCC, DWCC, Platelet count, PDW

Data for 2005 confirms previous observations that the Hemocue check on donors who fail the copper sulphate test reliably identifies donors with acceptable Hb levels for donation. Autoanalyser results on venous samples showed that about half of the donors who fail both copper sulphate and Hemocue had Hb levels above the acceptance threshold representing about 2.3% of donors (1488/65,838).

Examples of analyses which could be undertaken on this large dataset are:

- Population estimates of Hb by gender, age and donation history etc.
- Estimate of impact on Hb deferrals of varying Hb cut points for donation

- Impact of policy on donor return behaviour
- Sensitivity & Specificity of CuSO₄ / other screening tests
- Testing of prediction models for the presence of iron deficiency

The work required to enable analysis to commence is to

- link the Sysmex output data & PULSE data sets,
- define the combined dataset; update as required,
- clean the data, Define the initial analyses,
- extract the data
- run and report analyses.

The resources required to take this forward have been initially defined as: capacity to extract the relevant donor and donation data from Pulse for linkage - data analyst and programming skills - capacity for validation, storage and manipulation of the data, and specialist statistical input. The requirements can be split into (a) making the data from 2005 to the present available for analysis and (b) to establish a production system for ongoing data management. The latter would be important to provide the flow of data required to evaluate the outcomes of a planned change in selection procedures.

Dr Moji Gesinde

Are there safe and effective haematinic regimes? Do these enable more frequent donation?

A large Australian Red Cross study (2003) provides data on the prevalence of iron deficiency (defined as serum ferritin <12ug/ml) in male and female donors and in the general population. With the use of lower Hb acceptance thresholds, the proportion of iron deficient donors was slightly higher.

<i>Hb Threshold for donation</i>	<i>Iron deficient donors</i>
Males	
128g/l	6.2%
130g/l	6.0%
135g/l	5.3%
Females	
118g/l	22.0%
120g/l	20.6%
125g/l	18.9%

Iron supplementation (100mg Fe daily) in red cell apheresis donors donating a total of 7 double units at intervals of 8-10 weeks with a predonation threshold of 140 g/l was effective in maintaining serum ferritin levels, indicating that iron absorption was high, estimated to be 8%.

In a study on 526 donors randomised to receive a multivitamin preparation including ascorbate, folate and cyanocobalamin providing a daily dose of no iron (placebo), 20mg or 40 mg of iron, males donated 4 times at 2-month intervals and females 3 times at 3-month intervals. Serum ferritin levels fell in the placebo arm and remained stable or rose in the 20

and 40mg arms. A daily 20 mg dose of Fe appeared adequate to maintain serum iron levels, at this rate of donation.

Downsides of a wider use of iron supplementation for donors include poor compliance, the need to avoid inappropriate use of iron on HFE C282Y homozygotes and the risk to children of iron poisoning. The use of 20 mg (over the counter) iron preparations may reduce the poisoning risk

Crispin Wickenden

Donor attendance frequency

NHSBT data: - requested by Chair and kindly provided by CW after the workshop

Whole Blood Donors – Gender and Donation Frequency Distribution

<i>Donations in 2007/08</i>	<i>F</i>	<i>M</i>
1	297,019	222,980
2	203,710	183,853
3	90,539	110,326
4	2,699	4,321

To expand the data presented by Dr Gillon, more data is needed to show how many donors reattend but are deferred for low Hb on second and third donations within (e.g.) 1 year.