

# Hemochromatosis and blood donation

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## “Hemochromatosis and blood donation”

Abstract

### **Background:**

The voluntary, unpaid, altruistic blood donor is a cornerstone of current transfusion medicine. The complexity of medical and ethical issues related to blood donation and hemochromatosis has led to a large number of studies related to the safety of the hemochromatosis donor and the quality of the blood components produced from these donations. The issue of accepting persons with HC as blood donors is diverting, both in Europe and worldwide and without joint guidelines.

### **Study design and methods:**

A questionnaire-based study was performed and mailed to all 25 blood bank leaders in Norway. Descriptive analysis was used to evaluate the data.

### **Result:**

Eight of 22 blood banks followed national guidelines concerning persons with hemochromatosis strictly. Other blood banks make local adjustments. 16 of 22 responding blood banks accept hemochromatosis donors and five do not, and one answered partly yes. The reasons the blood bank leaders forward supporting the acceptance of hemochromatosis donors differ.

### **Conclusions:**

Based on published papers and the present questionnaire, we believe that a clear definition of the “hemochromatosis donor” and guidelines with more detailed information on acceptable donation regime would be important to overcome the weak points in blood donor eligibility criteria.

Key words: hemochromatosis, blood donor, motives, eligibility criteria, Norway

## Introduction

The voluntary, unpaid, altruistic blood donor is an important part of transfusion safety (1-4). Nevertheless, under some circumstances other options may be both needed and beneficial since the blood bank availability is not equally distributed throughout the world (5). In general, blood donation should be for the benefit of the patient, not for the donor (3, 6). Regardless of donor motives, the blood donation causes significant iron loss, and it has been a long-lasting medical issue if iron depletion could reduce risk of contracting diseases as myocardial infarction (7, 8). Such possible advantages of blood donation have not raised any storm of “self-care motivated” donors although “pure altruism” may not be sufficient to define donor motivation (9).

For persons with diagnosed iron overload – hemochromatosis – the situation is different. Despite substantial disagreements concerning “safe” s-ferritin concentration limits (10), bloodletting is unanimously the therapy – or prophylactic measure - of choice (11, 12). The possible ethical conflicts are accordingly obvious; the hemochromatosis blood donor may have financial benefit by donating free in a blood center rather than paying for the same service in an outpatient clinic (3, 4). In addition, many patients with hemochromatosis want frequent bloodletting although the treating physician does not find this indicated (10, 12, 13). Accordingly, it could be argued that blood centers should defer donors with hemochromatosis (6).

The issue of accepting persons with hemochromatosis as blood donors is nevertheless much more diverted (3, 14). Firstly, the definition of the term hemochromatosis vary. Iron overload is mostly due to HFE-gene mutations (15-17). The term preclinical hemochromatosis indicates that there is only an elevated s-ferritin concentration and the condition is named clinical hemochromatosis when organ-injury is diagnosed. Due to extensive screening programs and knowledge on familiar occurrence, many people know that they have iron overload or they are at risk of developing iron overload. Thus, new blood donors may be motivated by knowledge on a personal risk of having iron overload– and registered blood donors may be diagnosed through the blood centers’ screening program.

The complexity of medical and ethical issues related to blood donation and hemochromatosis has led to a large number of studies concerning the safety of the hemochromatosis donor, and the quality of the blood components produced from these donations (11, 14, 18). The hemochromatosis donor exposed to the normal selection program for blood donor does not

seem to represent any additional risk of transmitting an infection to the patient (18, 19). In addition, the quality of the blood components produced from donors with iron overload is not inferior to components produced from other donors. (15, 18, 20).

Based on published papers, the ethical dilemmas and multinational legal documents as the European Blood Directive (21), it could be anticipated that common acceptance criteria for donors with iron overload were available. In reality, the situation is heterogeneous as demonstrated by a world-wide survey in 2013(3).

Norway is a country with 5.2 million inhabitants. The blood transfusion service is decentralized and there are 25 hospital-based blood banks. The country has four health regions and there is formal and informal contact between the blood banks in each region. Only a minority of the blood donation sites has a transfusion medicine specialist working in the facility. To investigate the blood banks' practice concerning people with hemochromatosis, we conducted a questionnaire-based study with the primary aim to describe the situation for the hemochromatosis donor in Norway. Our secondary objectives were to evaluate if daily supervision by a specialist in transfusion medicine, size of the blood bank or geographical position (health region) influenced the policy as we hypothesized that these factors are relevant.

## Material and method

### Subjects and design

We performed a questionnaire-based study in November 2014, and mailed this to all 25 blood bank leaders in Norway. Blood bank size was categorized based on number of donations per year. Data was collected and analyzed through 2015. Descriptive analysis was used to evaluate the data.

### Questionnaire

The questionnaire consisted of 20 multiple-choice questions. It was possible to select more than one alternative for each question and to add comments. The purpose of the questionnaire was to collect relevant information concerning the policies of accepting persons with HC focusing on the aims of this study as described in the introduction.

Our main question focused on whether or not blood bank leaders accepted persons with HC as donors. If the answer was yes, follow-up questions clarified their reasons for the acceptance. If the answer was no, the respondents were asked to choose among various options for not accepting this blood donor. We also asked about the frequency of donations where persons with HC are accepted and if economic aspects could be of importance.

A draft of the questionnaire was validated by three specialists in transfusion medicine and by research colleagues with expertise in survey methodology. Corrections of the questionnaire included some new questions and rephrasing several others.

### Ethical concerns

The study complied with the Declaration of Helsinki and was submitted to the Regional Committees for medical and health research ethics of Western Norway (REC) as a disclosing evaluation. The respondents were invited to participate as leaders of the blood bank. The invitation contained information about the project and by responding to the survey, they gave their informed consent. No approval by NSD (Norwegian national institution for data security in research) was needed.

### Results

Leaders from 22 of 25 blood banks (88%) from the four health regions of Norway participated. The participating blood banks were divided into small, medium and large, separated by number of donations per year: S = small, < 1000 donations per year, M = medium 1000-9999 donations per year, L = large 10000+donations per year. An overview of responses is presented in Table 1. Descriptions of the accepting blood banks are presented in Table 2. Comments from each participating blood bank are reported separately.

**Table 1**

TABLE 1 Descriptions of results from questionnaire. Number of participants and size of participating blood bank at each Health Authority. HC = hemochromatosis. RHA = Regional Health Authority in Norway

Regional Health Authority (RHA) in Norway		Northern RHA N=8			Central RHA N=3			Western RHA N=3			South-Eastern RHA N=8		
Size of blood bank	Sum	S	M	L	S	M	L	S	M	L	S	M	L
Is your blood bank covering other hospitals?													
Yes	10			1		2			2	1			4
No	11	4	2	1			1					2	1
Partly yes	1												1
Do you have common criteria for accepting blood donors having HC, within your health region?													
Yes	10			1		1			2	1		2	3
No	3					1	1						1
Partly yes	9	4	2	1									2
How do you define HC?													
Ferritin cons >1000µg/L	2									1			1
Genetic test homozygosity for C282Y	5	1							1				3
Excess ferritin and homozygosity for C282Y	9	2	1			1			2			1	2
Excess transferrin-saturation	2								1				1
Clinical symptoms or organ damage	0												
Ferritin above limit	2		1	1									
Other	7	2				1	1					1	2
Is your blood bank accepting HC persons as donors?													
Yes	16	2	2	1		1	1		2	1		2	4
No	5	2				1							2
Partly yes	1			1									0
Is your blood bank using Norwegian guidelines (Veilederen)?													
Yes	8	1	2			1			1			2	1
No	1												1
We do not accept HC persons as blood donors	5	2				1							2
Partly yes, with local adaptations	8	1		2			1		1	1			2
Reasons for accepting HC persons as blood donors?													
Shortage of donors	1											1	0
Unethical not to use this blood	7	2		1			1		1	1		1	0
No reasons not to use this blood	10	2	1	2			1			1		2	1
Not increased risk for infectious disease	10	2	1	1					2	1			3
Excess ferritin-concentration	0												
Benefit for the donor	0												
No reason to believe that these donors are dishonest	10	1	2	1					1	2		1	2
Reasons for rejecting HC persons as blood donors?													
We do not accept persons with a disease as donors	2	1											1
Increased risk for contaminated blood	0												
Not the right motivation for donation	3												3
Economical motivations	1												1
Early organ damage	0												
Dishonest answers	2					1							1

As shown in Table 1, there is a considerable variation in how the hemochromatosis donors are treated in Norwegian blood banks. In general, 16 of 22 responding blood banks accept hemochromatosis donors. Eight of 22 blood banks follow national guidelines concerning persons with hemochromatosis strictly. Other blood banks (15) make local adjustments, 1 blood bank reports not to comply with the guidelines and 5 blood bank answers that the hemochromatosis persons are not accepted as donors.

The reasons for accepting hemochromatosis donors differ (see Table 1) but a common denominator is that no risk of “infectious blood” is recognized.

The blood bank leaders advocating hemochromatosis donor deferral highlight the aspects of donor motivation; a person with hemochromatosis may not have “correct motivation” and the need for bloodletting may cause dishonest answers. Some key statements are cited within the frame below the result part.

Table 2 shows that also among the blood banks allowing persons with hemochromatosis to donate, there are substantial differences concerning blood donation policies. Nine blood banks allow more frequent donations from persons with hemochromatosis.

**Table 2**

Description of results from 17 blood banks where HC persons are accepted: frequency of donations, access to supervision, size of blood bank, and geographical position/health region. Regional Health Authority in Norway = RHA

Are HC persons donating more frequently?	Access to donor physician?	Northern RHA N = 6	Central RHA N = 2	Western RHA N= 3	South-eastern RHA N= 6
Yes n= 9	Full time donor physician n = 5			1 Medium 1 Large	1 Medium 2 Large
	Part time associated physician n = 4	1 Small 1 Medium		1 Medium	1 Large
No n = 8	Full time donor physician n =3	1 Large	1 Large		1 Large
	Part time associated physician n=5	1 Small 1 Medium 1 Large	1Medium		1 Medium

According to Table 1, the size of the blood banks does not seem to influence the question of donor acceptance. Two of the largest blood banks in Norway do not accept hemochromatosis donors. The table does not specify the blood banks with full time physician but as the transfusion medicine experts mostly work at the largest blood banks, these findings overlap.

The results provided in Table 1 also reveal that there are considerable differences in donor acceptance between blood banks belonging to the same health region. The only question answered with full agreement was that all blood banks in Health region Western Norway accept hemochromatosis donors.

Table 3 shows that the statement in the Norwegian guidelines concerning a cost-neutral alternative for blood donors with hemochromatosis is interpreted differently.

**Table 3**

Is there a cost neutral alternative for the HC donor?

Is there a Cost neutral alternative?	Northern RHA N= 8	Central RHA N=3	Western RHA N= 3	South-eastern RHA N= 8
Yes	2	1	2	3
No	1	1	1	2
Partly yes	2			2
Do not know	3	1		1

### Key statements from respondents

#### Reasons for accepting HC persons as blood donors

- It is unethical to shed blood that can be used by patients
- No greater risk of infection than blood from normal blood donors
- No reason to believe that people with hemochromatosis do not want to answer as honestly as other donors
- There is no reason to discard the blood

#### Reasons for not accepting HC persons as blood donors

- Persons with HC have “wrong” motivation for being a blood donor
- HC is considered a disease and we cannot approve sick persons as donors
- Blood donors might not be honest in answering the questionnaire
- Blood donor may have a financial motive

## Discussion

Several studies have documented that the guidelines concerning hemochromatosis patients as blood donors differ significantly also between neighboring countries (3, 4, 11). Different interpretation of the term “volunteer, non-remunerated donor” is the most controversial issue (6) but also the various definitions of hemochromatosis make decisions difficult. The terms “clinical hemochromatosis”, “preclinical hemochromatosis”, “biochemical

hemochromatosis”, “risk person for developing iron overload”, “homozygous hemochromatosis”, “heterozygous hemochromatosis” and “compound heterozygous” are all used. This rather unprecise terminology seem to create uncertainties within the blood bank communities, as illustrated by the different definitions used by the blood bank leaders participating in this study. The subject is also truly complex, as e.g. results of genetic analyses may not predict disease (22, 23).

As shown in the tables, the Norwegian blood banks’ hemochromatosis donor policies are “heterogeneous”. Seventeen of 22 blood banks accept blood donors, and five do not. The situation is thus corresponding to reports from Switzerland (4) and results from an international survey (3). The data presented in Table 1 shows that our hypothesis that intra-regional acceptance criteria would be similar is not correct. Apart from Health Region Western Norway (response rate 75%), there is not agreement on donor acceptance within any health region. Because there are several differences in definitions of hemochromatosis, we postulated that blood banks with easy access to medical expertise would have a uniform donor acceptance policy. As shown in Table 2, also this hypothesis was proven to be wrong. Among the eight blood banks with a specialist in Immunology and Transfusion Medicine, five blood banks accepted hemochromatosis donors and three did not. Again, between these blood banks, the definition of hemochromatosis varied, also reflected in the blood banks’ different policies for referring new donors with high s-ferritin concentrations to further clinical evaluation (results not shown). Similar differences may be found regarding screening for hemochromatosis in a general population (24).

Due to their increased iron uptake, hemochromatosis donors are often allowed to donate more frequent than other donors, based on individual evaluation by a physician. Five blood banks with donor physician allowed increased donation frequency, and three did not.

Table 1 also summarizes the reasons for accepting or not accepting hemochromatosis donors. The main arguments to include these donors are that there is no evidence showing that they have dishonest motivation for donation, no “secret” threat to the blood supply and no proved evidence for increased risk related to transmission of infectious diseases. These statements are in line with arguments proposed in several papers advocating use of blood from hemochromatosis donors (14, 18).



The main arguments given to exclude hemochromatosis donors are related to donor motivation, risk of dishonesty during the donor interview and a general attitude not to include donors having a disease (23). The financial benefit, by not having to pay for outpatient treatment, was only mentioned by one responder. The Norwegian guidelines state that if the persons with hemochromatosis are accepted as donors, there should be a cost-neutral alternative. This alternative is however not defined, and the statement is interpreted differently as documented by the answers provided in Table 3. We believe that the intention of this statement is that if a hemochromatosis blood donor is temporarily deferred, the donor should have access to free “therapeutic donations” if necessary during this period, as suggested by Brailsford et al (25).

In a time with harmonization of guidelines and focus on evidence-based practices, it is not acceptable that the same potential blood donor should meet different acceptance criteria from neighboring blood banks. In a broader sense, also the international blood bank community should be able to find consensus (11). Based on published papers and the present questionnaire, we believe that a clear definition of the “hemochromatosis donor” and guidelines with more detailed information on donation regimen are important to standardize the blood donor eligibility-criteria. The donor eligibility criteria must also be fair to the donors (25).

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