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Review

Donor health assessment – When is blood donation safe?☆

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ABSTRACT

Blood donation is a highly regulated practice in the world, ensuring the safety and efficacy of collected blood and its components whether used as irreplaceable parts of modern transfusion medicine, as a therapeutic modality or additional support to other clinical therapies. In Norway blood donation is regulated by governmental regulations ("Blodforskriften") and further instructed by national guidelines, "Veileder for transfusjonstjenesten" [1], providing an aid for assessment of donor health. This concise review touches upon: definitions of donor health and disease; some important pitfalls; and the handling of some common and less common pathophysiological conditions; with an example from the Blood center of Oslo University Hospital, Norway's largest blood center. I also comment on some medications used by a number of blood donors, although wounds, ulcers and surgery are not included. Considering the panorama of conditions blood donors can suffer from, blood donation can never be completely safe for everybody, as zero risk does not exist, but it is our task through donor evaluation to identify and reduce risk as much as possible.

1. Introduction

The purpose of the blood service is to provide patients with safe blood components as needed. The blood service should also provide a high level of protection for blood donors. The guidelines therefore include the most important physiological criteria for protection of the blood donor. First of all, the blood donor should be healthy. Furthermore, the blood donor should be above 18 years old, weigh more than 50 kg and have a normal blood pressure (above 100/60, below 180/100 mm Hg). The heart rate should be between 50 and 110 beats per minute and hemoglobin levels should exceed 12.5 g/L for women and 13.5 g/L for men. Donors in need of iron supplementation should be advised to take oral iron medication.

2. Who is healthy?

The word "healthy" can mean several things. "Health" is by the WHO defined as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [2]. Alternatively, and a lot more useful, the word may be defined as "the ability to adapt and manage physical, mental and social challenges throughout life" [3]. As such, used by common people the word can include a range of "everyday problems". This is also shown in a lot of book titles ranging from "Get well with yoga", "Healthy food and workout", "Healthy due to herbs", "Healthy fat" and "Unexplainably healthy – nine keys to spontaneous healing". On the other hand, book titles like "Neither ill nor healthy" and "Healthy and chronically ill" introduce a doubt – can one really be sure. Perhaps it is true, as has been suggested, that a healthy person is just not investigated well enough. Still, if you feel generally healthy, you should be able to donate blood. In the blood center, we have informed the donors that they should only donate when they feel healthy. Of course, many donors are very motivated and feel obliged to donate when they receive the automatic call from us – sometimes they may ignore small symptoms or trivial problems that have become habitual to them. Many people live with stable, benign conditions that may be revealed in the blood center, e.g., the irritable bowel syndrome, arthrosis or allergies.

The value of an "abnormal" blood test in an otherwise healthy person, is questionable. The reference interval for a test result is defined as the interval containing results from 95% of healthy individuals, this implicates that 5% may have a "pathological" value without having an identifiable medical condition. Similarly, one out of 20 lab tests analysed will per statistical definition give a deviating result in a "normal" sample. In addition, many people will have "normal" lab values while suffering from mild medical conditions.

3. Disease

A "disease" is "a particular abnormal condition that negatively affects the structure or function of part or all of an organism, and that is

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not due to any external injury" [4]. Diseases can be general or local, acute or chronic. Factors influencing disease include "disease feeling", disposition to disease and the way the patient "copes with" the condition.

4. How do we obtain information about donor disease?

Several questions in the blood donor questionnaire provide key points about the blood donors' medical history. Based on these, the interviewer has an important function in revealing conditions that are important to blood donation, even though unrecognized by the donor. It is also important to clarify whether the donor has understood the questions in the intended way. If the donor admits recent contact with health care, without being able to explain properly what was done/concluded, we sometimes ask for consent to call for medical information to help us decide upon eligibility for blood donation. Although individual assessment occupies considerable medical resources, we appreciate the opportunity to maintain donor safety and service, and at the same time maximize the number of donors in our blood center.

Before first donation and with regular intervals, donor heart rate and blood pressure are checked, which sometimes gives information about pathological conditions. There may also be other obvious signs of disease. In these cases, donors are recommended to see their general practitioner (GP) for further investigation.

Information about donor conditions is often lost and the causes for this can be numerous. The donor may misunderstand our questions, forget to inform us, consider it unimportant or may not understand that their problem can be significant under special conditions. Also, there may be conditions the donor is not aware of, or does not want to disclose [5]. In most cases, the missing information is not vital, but we should remember the fact that communication with other people always brings the risk of misconceptions.

5. Mental disorders

A person with an obvious psychological problem should not be accepted as a donor if there is doubt about the validity of the medical information the donor provides about him/herself, in the present or past. Conditions that we fear to impair donor information include bipolar disease, attention deficits, depression and similar problems. The pharmacological treatments for these may also cause harmful side effects in some cases. Some anti-psychotic medications can cause arrhythmias, for example. We see increasing prescription of anti-psychotics for insomnia, and may speculate: is this person being frank about the diagnosis? And how important is it for blood donation to sleep well at night? Not to mention the problem of self-medication in certain groups.

6. The disease list

Attached to the guidelines [1] we find a list of conditions and how to handle these. However, the list is not complete, not updated, and for some conditions, it is hard to understand the reason for the recommendations. Blood centers with medical doctors make individual decisions, and gradually different strategies for donor consideration have developed. There is a real need for the revised edition, coming next year. It is expected to include more medical conditions and recommendations, hopefully reducing the need for individual clinical assessment. In the future, we hope the guidelines will be continuously updated electronically.

A list of common questions to the blood center physician is shown in Table 1.

7. Some welcome changes

Both the national guidelines [1] and local procedures have been changed recently, to allow inclusion of a number of new donors at Oslo Blood Center.

7.1. Allergy

Deferral of allergic persons has been changed to allow donors with a history of more serious allergic symptoms, and now only anaphylactic reactions provide reason to deferral. Hives, drug-induced eczema and other atopic symptoms are now accepted, as long as the donor is free of symptoms on the day of donation, with anti-histamine medication if necessary. Having an Epi-pen is not a deferral reason by itself, since these are also prescribed following strong but non-anaphylactic reactions.

7.2. Antihypertensive medication

For 3 years we have allowed donors taking anti-hypertensives like calcium channel blockers, diuretics, ACE-inhibitors and AII-antagonists, as long as the blood pressure is now stable, the donor has no serious side effects and is being controlled by the GP. ACE-inhibitors and AII-antagonists are not allowed in apheresis donors due to the proposed risk of bradykinin-induced hypotension [6]. We still do not allow beta-blockers, but data from other blood centers indicate that this is safe (Magnussen, K. and Kronborg, J., personal communication). We have presented data about these donors in abstract form [7].

7.3. Donors above 70 years of age

Removing the upper age limit has allowed a number of healthy elderly people to continue to donate until a health problem occurs. A study will shortly be initiated to quantify the effect of this change.

7.4. Patients with haemochromatosis

In cooperation with the hematology and internal medicine policlinics we accept prospective donors who are successfully treated by venesection and in need of maintenance treatment. They must be otherwise healthy and their ferritin levels must be controlled by the responsible clinician. We let them donate 4 times annually, but inform thoroughly about the importance of respecting regular quarantines for other reasons.

7.5. Donors with previous drug abuse (not injecting)

National guidelines were revised so that only people who had been injecting drugs had to be permanently deferred. Cannabis use and oral/nasal intake more than one year back is now accepted if the donor presents with a stable/change of life style.

7.6. Men who have sex with men (MSM) and ex-prostitutes

It has been more than one year since MSMs were allowed in Norwegian blood centers, with a quarantine of 1 year after their latest sexual practice, as opposed to life-long deferral. The number of new donors following this change is very low.

7.7. Chagas' disease and malaria

Testing for these infections allows the inclusion of people from South/Latin-Americas and shorter deferrals following travel to malaria-countries (4 months rather than 12). The number of donors provided by this change is substantial; in 2017, 1600 donors were tested for malaria at our blood center, only 3 were reactive [8].

Table 1
Common questions regarding blood donor eligibility.

Asthma	Allowed if free of symptoms using inhalation medication. Systemic treatment with montelukast is also accepted.
Chronic Obstructive Pulmonary Disease (COPD)	Individual assessment (call medical information from treating doctor).
Allergy	Allowed if free of symptoms using local treatment or systemic antihistamines. See also text. Drug-induced rashes are usually not IgE-mediated.
Acne	Most regimes of peroral antibiotics can be accepted if effective.
CPAP	Donors with CPAP-support for sleep apnea are often more healthy after treatment than before. However, the "before" problem is often not revealed in the blood center.
Diabetes	Depends on treatment. Life-style changes: allowed. Anti-diabetics or insulin: not allowed
Epilepsy	Not allowed. An epileptic seizure in the blood center would be dramatic, and we fear criticism if it turns out that we bleed the person knowing about a history of epilepsy – even though many years had passed.
Cancer	Not allowed by the EU guidelines. Only exceptions are basal cell carcinomas of skin and HPV-induced carcinoma in situ of the cervix uteri. Often hard to explain these rules for people who have recovered from cancer.
Autoimmune diseases	Hypothyroidism: allowed if euthyroid on levaxin substitution treatment and controlled by GP. Some conditions of the skin with unknown cause are allowed: alopecia areata, vitiligo, lichen sclerosus/atrophicus (depending on size of affected area)
Degenerative diseases	Brain/retinal degeneration: not allowed. In general; little is known about the effect of blood donation on degenerative processes. These persons are deferred due to the benefit of the doubt. Polyneuropathic feet can pose an infection threat if the person can not feel that the skin is damaged.
TGA	Transitory global amnesia – no risk of repetition, allowed after 6 months.
Genetic disposition to disease	Problematic; consider type of disease. Individual assessment.
Heart disease	Congenital heart conditions, corrected operatively: assess prognosis, need for antibiotic or antithrombotic prophylaxis, control regimes, risk of later complications.
EKG changes	Incomplete right bundle branch block allowed [9], other arrhythmias not allowed.
Dynamic/flow irregularities	Individual assessment.
Ablation	Effective treatment of arrhythmias and atrial flutter, allowed after 2 years if no residual symptoms.
Stenosis of carotid artery	Diagnosed using ultrasound/Doppler: Allowed if no murmur/small stenosis
Sarkoidosis	A small portion of these patients recover fully. These are allowed after 5 years
Osteoporosis	Fear of fractures if reaction with syncope. Osteopenia and anti-resorptive treatment can be allowed
Fibromyalgia, Chronic Fatigue Syndrome (CFS)/Myalgic Encephalomyelopathy (ME)	Individual assessment. ME: allowed 2 years after recovery
Gastrointestinal	Irritable colon: consider risk of infection, fluid balance, and bowel inspection (what is normal for this donor, can running stools be distinguished from infectious diarrhea? Coeliac disease: if free of symptoms on diet and no sign of malabsorption
Gastroenteritis	Be aware of some infectious agents where asymptomatic carriers are common.
Bladder	Interstitial cystitis: hard to distinguish symptoms from acute cystitis. Urinary tract infection prophylaxis with hippuric acid can be allowed, as can treatment of overactive bladder
MRSA/ESBL/VRE	Internal bacteria which should not be present on skin with normal hygiene.
B12/other vitamin deficiencies	Inquire about indication, control regime/follow up. Common treatment for diffuse symptoms, is there a real deficiency? If injections, must be performed by doctor/nurse. Makes little sense to correct deficiency first and then bleed… Same reasoning around vitamin D.

8. Conditions detected at the blood center

Plasma ferritin level is controlled at the time of the first ordinary donation. A few donors have elevated levels and are referred to their GP for a more thorough investigation, with genetic testing of the most common point-mutation leading to haemochromatosis. These donors are welcomed back since their primary motivation to donate blood was altruistic. However, in some of these donors, the diagnosis cannot be established, while ferritin remains high. These are sometimes difficult to assess; if they are feeling well, it should be safe to let them donate, or what?

Positive DAT (Direct Antiglobulin Test/direct Coombs test) indicating the presence of autoantibodies on RBCs: these donors are found by accident (not a routine test for donors). They are deferred for 6 months, informed about symptoms of anaemia and when to seek doctor's advice. Sometimes the condition is temporary, if not, these donors are permanently deferred.

High numbers of WBC/RBC/platelets may sometimes indicate the presence of primary polycytaemias or other haematological diseases.

Lipaemic plasma may indicate hyperlipidaemia or hypercholesterolaemia, and slow filtration of full blood may be associated with thalassaemias or similar conditions.

Some donors have heart rates below the threshold of 50. Unless performing physical activity several times a week, these are a source of frustration. We worry about their tolerance to hypovolemia and risk of arrhythmia, and tend to send these to see their GP. However, it is important for the blood center employee to be able to distinguish the normal, respiratory variation in heart rate ("sinus arrhythmia") from a real arrhythmia, and also to recognize common extrasystolic contractions, these being common in healthy blood donors.

9. When the blood has been donated in spite of a risk

Neither cancer nor Lyme disease has ever been shown to be transferred by transfusion [10,11]. Still, we discuss each case in the department to assess if there is a risk for the patient and whether our clinical colleagues should be informed.

We encourage the donors to contact us if they experience symptoms in the days following donation. The common cold, the flu or a fever, gastrointestinal symptoms, most often represent viral infections. It is less obvious when symptoms are more diffuse, headache/tiredness/reduced general condition – what is due to infection and what may be due to the donation itself? It is always important to give the donor credit for returning this information.

We have observed that a cold may often debut during the days following donation. Whereas this is most likely to be a coincidence, it would be interesting to know whether the (extremely) temporary reduction of leukocytes that necessarily must follow, could open for the infection with a virus one otherwise would defeat…

Then how do we respond to information about possible infection risk? In most cases the blood is discarded, although we do individual assessments of symptoms and incubation times.

10. When the blood donor uses medication

Many potential blood donors use medications on a regular basis. Also, we commonly receive post-donation reports of medicines taken before donation, but not revealed in the interview.

Firstly, we consider the drug itself. Is the effect of the drug a problem for the receiver, or does it introduce a risk for the donor? What dose the patient is exposed to, is defined by the plasma volume in the blood product and the plasma concentration of the drug in the donor. As a rule, when 5 therapeutic halflifes ($T_{1/2}$) have passed, most drugs are reduced to negligible levels in the donor plasma [12]. Only very few medications can be harmful for prolonged time periods, such as retinoids. Furthermore, what is the indication for prescription? Is the donor having health problems he/she hasn't told us about? Does the donor experience side effects? Many drugs are not mentioned in the guidelines, either because they are too new, or because users would not logically present themselves in the blood center. But sometimes, physicians treat patients conditions with drugs registered for other indications, we have to ask. Some physicians find it necessary to prescribe uncommon medicines, not sold in Norwegian pharmacies and therefore hard to find information about, and also some people take unprescribed cures bought abroad or online.

Side effects are often relieved when the treatment has lasted for a few months, thus, we may advice to postpone donation to avoid these initial problems. However, an important point is that the donor should not stop taking medication to be allowed to donate blood. This could open for worsening of the patients problems.

Common drugs that we allow in the Blood center of Oslo, include antihistamines, thyroid hormone substitutes, antihypertensive drugs, drugs that lower cholesterol, proton pump inhibitors, antidepressants, sleeping pills and pain killers containing paracetamol (acetaminophen).

11. When is it safe to donate blood?

We can never guarantee that blood donation is perfectly safe for both the donor and the recipient. Our primary objective is to make sure the donation is as safe as possible, bearing in our minds that healthy people are coming to the blood center to donate their blood voluntarily and without remuneration. Health issues introduce an extra risk that the blood center physician needs to address, and we are responsible for the safety based on the information available. Due to the high numbers of donors admitted, a small individual risk may still induce a dramatic incident every now and then (see case box). If a donor who is accepted with a known, albeit low, risk, develops a problem that can be attributed to the blood donation, this would be highly undesirable.

Being a blood center physician means thinking about risk in a different way compared to our colleagues, and working to reduce this risk as much as possible for the benefit of both donors and patients.

11.1. Case box

Oslo Blood Center, 2015: Female in her thirties, previously donated blood > 5 times without any remarks in our files. Low ferritin found by GP in May, presents for donation in September, has eaten decently, hemoglobin 14.8 g/dL.

When bled for ca 350 ml, she goes into syncope with convulsions, ca 60 s. The donor is placed on a stretcher and moved to a separate room with continuous observation by a nurse, repeated control of heart rate and blood pressure. 1 h later, blood pressure is normalized, heart rate is low (118/68, 51). Donor is tired and nauseated, with little effect of antiemetic treatment (metoclopramide). Variable consciousness. Anamnestic information about several syncopes at home during activity is presented by a companion. The day after her previous donation she was picked up by an ambulance, however it is unknown what investigations were performed.

3 h after donation the donor is referred to local hospital for further observation. Under telemetric observation in hospital she is mobilized, and goes into asystole ca 10 s. Following stabilization she is immediately moved to the university hospital where she is instantly undergoing surgery and implantation of a permanent pacemaker. It turns out she had an underlying condition that predisposed to complications; complications that were provoked by blood donation.

12. Summary

Donor evaluation has developed to accept a plethora of benign conditions and medications used by donors, to fill the need for blood components in the western world. This is based on increasing knowledge and research, but also courage and willingness to accept some risk. In the future, we believe new methods will be developed to predict risk more accurately so that new groups can be included without compromising transfusion safety.

Conflict of interest

No conflict of interest declared.

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