Blood donation safety procedures: an overview

ASSIGN BUSTER

Qualification of blood donors has become a lengthy and detailed process, a ‘ donor inquisition’ some would say. Yet blood collection depends on this system of safeguards to protect the donor from injury and the recipient from the risks of allogeneic blood. Sensitive screening tests have been considered the cornerstone of blood safety for more than three decades. However, testing represents only one component of this system. Additional ‘ layers of safety’ include following measures:-

- Detailed donor education programmes prior to recruitment,
- Pre-donation informational literature,
- Stringent donor screening selection and deferral procedures,
- Post-donation product quarantine
- Donor tracing and notification when instances of disease transmission are detected.

Each element plays a role in preventing ‘ tainted’ units from entering the blood inventory. Most transfusion services have developed evidence-based standards and regulations for the selection of donors and quality systems to assure excellence in all phases of their application. Other standards derive from ‘ expert opinion’ and ‘ common sense’, and these policies need to be revisited as scientific information becomes available.

Blood donors should have the following general qualifications:-

- They should have reached the age of consent, most often 18 years, but 17 in some countries such as the USA and the UK;
- They should be in good health,
- They should have no history of serious illness,

- Must weigh enough to allow safe donation of a ‘ unit’ and not recognize themselves as being at risk of transmitting infection.

Ideally, donation should be strictly voluntary and without financial incentive. Some blood services impose an arbitrary upper limit on age, commonly 65 years, or up to age 70 in Denmark and the UK; however, it seems curiously subjective to exclude donors on the basis of age alone if they are otherwise in good health. The Blood Collection Service should provide informational literature for prospective blood donors.

After information and counselling about criteria for donor selection, donors should consent in writing to the terms of donation, including the use of the donated blood, the extent of testing, the use of testing results (including donor notification of positive results) and the future use of any stored specimens.

Donors should be told about the possibility of delayed fainting and about other significant risks of the donation procedure. Blood donation has potential medicolegal consequences. If a donor becomes ill shortly after giving blood, the illness may be attributed to blood donation For this reason, among others, it is important to ensure that donors have no history of medical conditions such as brittle diabetes, hypertension, poorly controlled epilepsy and unstable cardiopulmonary disease that might be associated with an adverse event following phlebotomy. Pregnancy might be adversely affected by the donation process and ordinarily excludes a donor. Donors who become ill within 2 weeks of donation should be encouraged to inform the transfusion service, which may wish to discard the donated blood, recall any plasma sent for fractionation or follow up recipients of the blood

components as appropriate. Donors who develop hepatitis or HIV infection within 3-6 months of donation should also inform the Blood Collection Service.

Donor interview

The donor interview should be conducted by staff trained and qualified to administer questions and evaluate responses. The donor interview should be conducted in a setting sufficiently unhurried and private as to permit discussion of confidential information.

With current practices in the USA, approximately 2% of volunteer donors still disclose risks that would have led to deferral at the time of donation. Introduction of standardized and validated questionnaires and the application of interactive computer-assisted audiovisual health history may reduce errors and misinterpretations during conduct of the donor interview.

Physical examination

Blood collectors perform a limited physical examination designed to protect donor and recipient. Screeners routinely assess the donor’s general appearance and defer those who do not appear well or are under the influence of alcohol. A normal range of pulse and blood pressure is defined, although variances may be granted for healthy athletes. Body weight and temperature are measured by some collection services. Both arms are examined for evidence of illicit drug use and for lesions at the venepuncture site.

Volume of donation

The volume of anticoagulant solutions in collection bags is calculated to allow for collection of a particular volume of blood, which, in the UK, is 450 ± 45 ml. In the USA often 500 ml, but in no case more than 10. 5 ml/kg including the additional volume of 20-30 ml of blood collected into pilot tubes. From donors weighing 41-50 kg, only 250 ml of blood is collected into bags in which the volume of anticoagulant solution has been appropriately reduced. In some countries, the volume collected routinely is less than 450 ml, for example 350-400 ml in Turkey, Greece and Italy, and 250 ml in some Asian countries such as Japan, where donors tend to be smaller.

Record-keeping

It should be possible to trace the origin of every blood donation and records should be kept for several years, depending on the guidelines for each country. In many countries, a system employing unique bar-coded eyereadable donation numbers is now in use. This system makes it possible to link each donation to its integral containers and sample tubes and to the particular donor session record. Information concerning previous donations, such as records of blood groups and microbiology screening tests, antibodies detected, donor deferrals and adverse reactions are important for subsequent attendances. Electronic storage of donor information greatly facilitates accurate identification, release, distribution and traceability of units of blood and blood products. An international code, ISBT 128, is intended to be used by all countries for the accurate identification of donors and donations. These records must be protected from accidental destruction, modification or unauthorized access.

Frequency of donors in the population

Although in many Western countries, some 60% of the population are healthy adults aged 18-65 years and thus qualified to be blood donors, the highest annual frequency of donation in the world corresponds to about 10% of the population eligible to give blood donating once per year, as in Switzerland. The frequency in most developing countries is less than 1% . The number of units collected per 1000 US inhabitants of usual donor age (18-65) was 88. 0 in 2001, up from 80. 8 in 1999. Although this number compares favourably with the rate of 72. 2 per 1000 in 1997, it pales in comparison with the 100 units per 1000 population collected in Switzerland. As treacherous as it may be to interpret these figures, the numbers suggest that US collecting facilities are progressively improving efficiency. Data from the American National Red Cross indicate that the average volunteer donates about 1. 7 times a year. Losses from outdated red cells accounted for 5. 3% of the supply but, given the fact that red cells can be transfused only to compatible recipients, the number of usable units outdated appears to be extremely small. More than 99% of group O units and 97% of group A units were transfused.

The shrinking donor pool: the safety vs. availability conundrum

Donor deferrals and miscollected units have an increasing role in blood shortages. In a 1-year study at a regional blood centre, nearly 14% of prospective donors were ineligible on the day of presentation and more than 3. 8% of donations did not result in the collection of an acceptable quantity of blood. Short-term deferral for low haemoglobin (Hb) was the

overwhelming reason for the deferral of female donors in all age groups, representing more than 50% of all short-term deferrals. In first-time female donors, low Hb accounted for 53-67% of deferrals within different age groups, and for repeat female donors 75-80% of deferrals. In both firsttime and repeat male donors aged 40 years and older, the most common reason for short-term deferral was blood pressure or pulse outside allowed limits. For persons aged 16-24 years, regardless of sex and donation status, the most common reason for lengthy deferral was tattoo, piercing or other non-intravenous drug use needle exposure. For 25- to 39-year-old female donors, needle exposure was also the most common reason, whereas for male donors, travel to a malarial area was more common. For all ages over 40, the most common reason for long-term deferral was travel to a malarial area. Measures introduced to increase blood safety may have the unintended consequence of decreasing blood availability. Results from demographic studies indicate that certain donor groups or donor sites present an unacceptable risk of disease transmission. For example, blood collectors no longer schedule mobile drives at prisons or institutions for the disabled because of the recognized high prevalence of transfusion-transmissible viruses.

Few would argue the risk-benefit analysis of these exclusions. More questionable were the temporary exclusions of US soldiers exposed to multiple tick bites at Fort Chaffee, Arkansas, and the lengthy deferrals of veterans who served in Iraq and Kuwait because of the fear that they might harbour Leishmania donovani, an agent infrequently associated with transfusion risk. Donors who have received human growth hormone

injections have been indefinitely deferred because of the possible risk of transmitting Creutzfeldt- Jakob disease (CJD); however, relatives of patients with ‘ sporadic’ CJD are still deferred in the US (except for preparation of plasma fractions) despite evidence of their safety. There have now been five case-control studies of more than 600 CJD cases, two look-back studies of recipients of CJD products, two autopsy studies of patients with haemophilia and mortality surveillance of 4468 CJD deaths over 16 years without any link to transmission by transfusion (Centers for Biologic Evaluation and Research, US Food and Drug Administration 2002). Although the impact of this deferral on the US blood supply has been negligible, the recent indefinite deferral of donors who resided in the UK for a total of 3 months or longer between 1980 and 1996, and the complicated deferral policy for residents and visitors to the European continent, designed to reduce a calculated risk of transmission of the human variant of ‘ mad cow disease’ (variant Creutzfeldt-Jakob disease, vCJD), has had a substantial impact, a loss of as much as 10% by some estimates, particularly on apheresis donors (Custer et al. 2004). Additional donor exclusions appear to be on the horizon.

Donor medications constitute another significant area of deferral losses. Certain medications, for example etretinate (Tegison), isotretinoin (Accutane), acitretin (Soriatane), dutasteride (Avodart) and finasteride (Proscar), have been identified as posing potential risk to transfusion recipients because of their teratogenic potential at low plasma concentrations. Such exclusions have little impact on blood safety but each shrinks the potentially eligible volunteer donor pool. More troublesome, although not as numerous, are donor deferrals resulting from false-positive

infectious disease screening tests. This problem has been recognized since the introduction of serological tests for syphilis. However, during the past 15 years, the introduction of new screening tests and testing technologies has resulted in numerous deferrals for ‘ questionable’ test results and either complex re-entry algorithms or no approved method to requalify such donors. Surrogate tests used for screening have proved particularly troublesome. However, even specific tests result in inappropriate deferrals. Of initial disease marker-reactive donations, 44% proved to be indeterminate or false positive. Each year an estimated 14000 donors are deferred from donating blood for an indefinite period because of repeatedly reactive enzyme immunoassay (EIA) screening tests for human immunodeficiency virus (HIV) and hepatitis C virus (HCV), and several hundred donors are deferred for apparently false-positive nucleic acid testing (NAT) results.

Registry of bone marrow donors

Voluntary blood donors are highly suitable to become bone marrow or peripheral blood stem cell donors for unrelated recipients, and many transfusion services now recruit them for this purpose. From its founding in 1986 until August 2003, the National Marrow Donor Program in the USA had registered more than 5 million bone marrow and blood stem cell donors, and Bone Marrow Donors Worldwide in the Netherlands records more than 8 million donors from 51 registries in 38 countries. Standards for acceptance of stem cell donors are based on blood donor eligibility. A uniform donor history is being developed.

Conditions that may disqualify a donor

Carriage of transmissible diseases

The most important infectious agents transmissible by transfusion are the hepatitis viruses B and C, HIV, human T-lymphotropic viruses (HTLVs), bacteria and the agents causing malaria and Chagas' disease. Increasing attention is being paid to the risks of 'emerging' agents and newly recognized infectious risks of transfusion such as West Nile virus, babesiosis and vCJD. Steps that should be taken to minimize the risk of infecting recipients with the agents of these and other diseases involve exclusion based on geographical residence, signs and symptoms of disease, high-risk activity and demographics associated with risk transmission. Donors who have been exposed to an infectious disease and are at risk of developing it should be deferred for at least the length of the incubation period.

Recent inoculations, vaccinations, etc.

To avoid the possibility of transmitting live viruses (e. g. those of measles, mumps, rubella, Sabin oral polio vaccine, yellow fever, smallpox), donors should not give blood during the 3 weeks following vaccination. In subjects immunized with killed microbes or with antigens (cholera, influenza, typhoid, hepatitis A and B, Salk polio, rabies, anthrax, tick-borne and Japanese encephalitis) or toxoids (tetanus, diphtheria, pertussis), the interval is normally only 48 h. These recommendations apply if the donor is well following vaccination. Plasma from recently immunized donors may be useful for the manufacture of specific immunoglobulin preparations. Donors who have received immunoglobulins after exposure to infectious agents should

not give blood for a period slightly longer than the incubation period of the disease in question. If hepatitis B immunoglobulin has been given after exposure to the virus, donation should be deferred for 9 months to 1 year; similarly, if tetanus immunoglobulin has been given, donation should be deferred for 4 weeks. When rabies vaccination follows a bite by a rabid animal, blood donations should be suspended for 1 year. In developed countries, tetanus and diphtheria immunoglobulin is derived from human sources. However, horse serum is still used in some parts of the world. Donors who have received an injection of horse serum within the previous 3 weeks should not donate blood because traces of horse serum in their blood might harm an allergic recipient. The administration of normal human immunoglobulin before travelling to countries where hepatitis A is endemic is not a cause for deferral.

Group O subjects may develop very potent haemolytic anti-A following an injection of tetanus toxoid, typhoid-paratyphoid (TAB), vaccine or pepsindigested horse serum, which may contain traces of hog pepsin. In the past, the use of such subjects as ‘ universal

donors’ sometimes led to severe haemolytic transfusion reactions in group A subjects. Platelet concentrates collected by apheresis from subjects with hyperimmune anti-A should not be used for transfusion to group A or AB patients in view of the large volume of plasma needed to suspend the platelet concentrate.

Ear-piercing, electrolysis, tattooing, acupuncture

All of these procedures carry a risk of transmission of hepatitis or HIV infection when the equipment used is not disposable or sterilized, and blood donation should then be deferred for 12 months. In the UK, donors are accepted if the acupuncture is performed by a registered medical practitioner or in a hospital. Although the association between tattooing and exposure to hepatitis C is generally acknowledged, less clear is whether a tattoo performed by licensed and inspected facilities carries more risk than a trip to the dentist’s surgery.

‘ Allergic’ subjects

Subjects who suffer from very severe allergy are unacceptable as donors because their hypersensitivity may be passively transferred to the recipient for a short period. Subjects with seasonal allergy (e. g. hay fever) may donate when not in an active phase of their hypersensitivity. A screening test for immunoglobulin E (IgE) antibodies would not help to identify those allergic individuals with an increased chance of passively transferring their hypersensitivity.

Blood transfusions and tissue grafts

Donations should not be accepted for at least 12 months after the subject has received blood, blood components or grafts. Increasingly, donors who have received transfusion in the UK are being deferred indefinitely as a precaution against transmission of vCJD.

Surgery and dental treatment

When surgery has been carried out without blood transfusion, donation may be considered when the subject has fully recovered. Uncomplicated dental treatments and extractions should not be a cause for prolonged deferral, as utensils are sterilized and the risk of bacteraemia persisting for more than 1 h is negligible.

Medication

Many subjects taking medication are not suitable as donors because of their underlying medical condition. Others are unsuitable as donors because the drugs they are taking, for example anticoagulants or cytotoxic agents, may harm the recipients. Subjects who have taken aspirin within the previous week are unsuitable when theirs are the only platelets to be given to a particular recipient. Ingestion of oral contraceptives or replacement hormones such as thyroxine is not a disqualification for blood donation. On the other hand, recipients of human growth hormone (non-recombinant) should be permanently deferred from blood donation as should subjects who have used illicit injected drugs. Deferral for specific medication use is usually an issue of medical discretion.

Donors with relatively minor red cell abnormalities

In some populations, a considerable number of donors have an inherited red cell abnormality. The three conditions most likely to be encountered are: glucose-6-phosphate dehydrogenase (G-6-PD) deficiency, sickle trait (HbAS) and thalassaemia trait. G-6-PD deficiency. This is the most common red cell enzyme defect; hundreds of molecular variants have been catalogued. Although most G-6-PD-deficient red cells have only slightly subnormal

survival and lose viability on storage with adenine at only a slightly increased rate (Orlina et al. 1970), some enzyme variants render the cells unsuitable for transfusion. With the African variant GdA- present in 10% of African Americans, a relatively small number of red cells are severely affected. However, the Mediterranean variant GdMediterranean and others render the red cell particularly sensitive to oxidative stress. If the recipient of one of these units develops an infectious illness or ingests fava beans or one of any number of drugs (phenacetin, sulfonamides, vitamin K, primaquine, etc.), rapid destruction of the donor's G-6-PD-deficient cells may result. Neonatologists avoid using G-6-PD-deficient blood for exchange transfusion, and subjects who have evidenced G-6-PD-related haemolysis should be permanently deferred from donation (Beutler 1994).

Sickle trait (HbAS).

Sickle trait red cells survive normally in healthy subjects, even after storage. However, in patients subject to various types of hypoxic stress, these cells survive poorly. HbS polymerizes at low oxygen tension and the cells are trapped in the spleen. Blood from donors with sickle cell trait should not be used for infants or for patients with sickle cell disease who undergo exchange transfusion. Patients, other than those with sickle Hb, who require general anaesthesia should have no problems if transfused with HbAS red cells provided that adequate oxygenation is maintained. Red cells from subjects with HbAS are usually unaffected by collection via apheresis, but those with sickling haemoglobinopathies should not donate by apheresis and are not suitable for intraoperative salvage. If blood from donors with sickle cell trait is glycerolized for storage in the frozen state, extra wash solution

must be used during the deglycerolization procedure. Sickle trait prevents effectiveWBC reduction by filtration.

Thalassaemia trait

This is associated with little or no reduction in red cell lifespan in most subjects with a normal Hb concentration and these subjects may be accepted as donors.

Special conditions in which normally disqualified donors may donate

In some circumstances, a donor may give blood or components to be used for a special purpose, even although the requirements for normal donation are not met. For example, a donor who is mildly anaemic or who has recently given birth may give plasma or platelets by apheresis; the plasma may be needed for reagent preparation, for example HLA antibodies, or the platelets may be needed for transfusion to the newborn infant. Donors at risk for carrying malaria may give plasma for fractionation. The usual interval between donations may be waived for important medical indications. The donor age limitation and a number of other screening criteria may be modified for components directed to the recipient of the donor’s bone marrow. In every case, medical evaluation should ensure that there is no increased risk to the donor’s health and that the value of the component outweighs any perceived increase in risk. Under these circumstances, informed consent regarding the variance and documentation of the circumstances is mandatory.

Donation of whole blood

Frequency of donation

The volume lost from a single unit donation is replaced within 48-72 h. Red cell mass recovers more slowly, requiring 3-6 weeks. Some collection services bleed donors no more than two or three times a year; most do not bleed women who are pregnant or those who have been pregnant within the previous 6 weeks. The primary objective of this policy is to protect the donor from iron deficiency. There is a wide variation in the recommended minimum interval between donations. For example in the US, in line with World Health Organization (WHO) recommendations, the interval can be as short as 8 weeks and a maximum of 3 l of blood per year may be collected. Premenopausal women should not donate as frequently as men. In the Netherlands, men are bled every 3 months and women every 6 months. Because few red cells are lost during platelet and plasmapheresis, these procedures may be performed more often and at shorter intervals. Standards vary by country; in the USA plateletpheresis donors may be drawn every 48 h up to twice per week and 24 times per year. Commercial plasmapheresis donors are bled even more frequently; however, physical examination is more rigorous and laboratory testing more extensive for these donors. As combinations of components, such as two-unit red cells, are drawn by apheresis, volumes and intervals become individualized, but generally limited by the loss of red cells.

Hb regeneration after normal blood donation

In 14 normal healthy subjects bled of about 400 ml of blood (8% of their blood volume), circulating reticulocytes increased minimally but significantly and peaked on the ninth day after bleeding. The Hb level was lowest 1 or 2 weeks after bleeding, and increased rapidly thereafter, reaching predonation levels at 3-4 weeks (Fig. 1. 1). In a study in which total red cell volumes were measured in subjects who had donated about 190 ml of red cells, about 50 ml of red cells were restored after 1 week and restoration was almost complete at 6 weeks.

Potential health benefits of blood donation

For the volunteer donor, the chief benefit lies in the satisfaction of selfless concern for the welfare of others. However, two studies suggest that there may be more tangible health benefits, particularly for middle-aged men, such as lowering the risk of cardiovascular disease. The proffered explanation derives from the so-called ‘ iron hypothesis’: menstrual iron loss protects women against cardiovascular disease; iron stores correlate with cardiovascular disease across European populations and heart failure is a hallmark of disorders of iron surplus (Sullivan 1981). One proposed mechanism for this association is generation of oxygen free radicals that induce oxidation of lipids. However the Johns Hopkins Hospital autopsy registry found less coronary artery disease in hearts from patients with haemochromatosis and haemosiderosis than in hearts of age- and sex-matched controls.

Salonen and co-workers (1998) conducted a prospective 9-year follow-up study of 2862 men aged 42-60 from eastern Finland, who had participated in

the Kuopio Ischemic Heart Disease Risk Factor Study. Only one man out of 153 who had donated blood in the 24 months prior to baseline examination suffered a myocardial infarction, compared with 316 (12. 5%) of the 2529 non-donors. Meyers and co-workers (1997) compared the rate of cardiovascular events of 665 blood donors with that of 3200 non-donors in a telephone survey of a cohort selected from the Nebraska Diet Heart Survey. By multivariate analysis, non-smoking men who had donated at least once in the previous 3 years had a significantly lowered risk of cardiovascular events; no additional benefit was derived from longer or more frequent donation.

Directed donations are those given exclusively for named patients, usually by relatives or friends. The use of directed donations contravenes the normal principles of voluntary blood donation, fails to increase safety and finds medical justification in vanishingly few circumstances:

- in patients with rare blood groups when the only available compatible donors may be close relatives;
- in occasional patients awaiting renal transplants, for whom donor-specific transfusions may still play a role;
- in infants with neonatal alloimmune thrombocytopenia or haemolytic disease of the newborn, for whom maternal platelets or red cells are occasionally invaluable;

(4) in children requiring open-heart or extensive orthopaedic surgery, for whom the total requirements for blood and components can be collected preoperatively, as for autologous transfusion but from designated relatives

or parents, thus minimizing the number of donor units to which the children are exposed in patients with leukaemia in relapse after bone marrow transplantation, for whom donor leucocytes are used as adoptive immunotherapy to induce graft-versusleukaemia (GvL) effect.

The practice of transfusing parental blood to premature newborn infants is not without risks. Mothers may have antibodies against antigens (inherited from the father) on the infant’s red cells, platelets or white cells and maternal plasma should not be used. Fathers should not serve as cell donors because they may have antigens present on their red cells, which are incompatible with maternally derived antibodies present in the fetus. Moreover, in view of partial histocompatibility, transfusion of cells from parents and close relatives may result in graft-versus-host disease (GvHD) in the infants, or older children, especially if the infants are immunodeficient. Circumstances such as these, in which blood or platelet suspensions should be irradiated, are described in. The practice of transfusing parents with blood from their offspring can also be dangerous.

Fatal GvHD occurred in two immunocompetent adult patients who were transfused with fresh whole non-irradiated blood from their children during cardiac surgery. In both cases, one of the donors was homozygous for one of the recipient’s HLA haplotypes. When such transfusions are indicated, and except for instances in which adoptive immunotherapy is intended, the components should be treated with 25 Gy gamma irradiation. People who donate for friends and family lose their anonymity and may be subject to influences not placed upon community donors. Such donors may provide less than candid answers to sensitive donor questions, either because they

believe that unsafe blood will inevitably be detected by testing procedures or because they wish to conceal information from the recipient or the blood collector.