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Blood Matters

Quarterly information for hospitals served by the National Blood Service

NATIONAL BLOOD SERVICE

NHS

Editorial

The Chief Medical Officer for England has highlighted the 'precious gift' of freely donated blood, and the theme of this issue is how conditions affecting blood donors can affect patients. It is hoped that this will increase awareness among blood users of the commitment made by volunteer donors, the implications for them of some of the initiatives that have improved safety for patients, and the duty of safe and appropriate use of their altruistic gift.

It also gives me an opportunity to exercise one of my hobby-horses, which is that blood donors are NOT patients. This may seem to state the obvious, but medical professionals have a natural tendency to 'medicalise' the world. In this way, some Blood Service doctors have in the past tended, and somewhat inappropriately, to regard their 'clients' (donors) as 'patients' with whom they have a 'caring' professional relationship (even to the extent of resuscitating them with adrenalin if they faint, something which is not allowed now!). Although the NBS has a clear duty of care to donors, this is because of the potential for harm to which donors are exposed whenever they give blood. This is very different from the situation of patients receiving medication (including blood products) prescribed by doctors. Indeed the duty of care impels 'donor clinicians' to do their best to stop blood donors becoming patients.

This dichotomy can be seen when patients undergo successful therapy for life-threatening disorders, such as cancers. In the flush of success they may get the message to 'live a normal life' – and what better way to live life and demonstrate health than becoming a blood donor? Although these are really examples of 'patients not being donors', what better way to get demoralised and upset than by being deferred as a blood donor? Deferral (i.e. 'refusal' or 'rejection') is a most unpleasant experience for any altruistic person; Blood Services do so without good reason at their peril.

Another example is the problem of those donors who give blood so frequently that the NBS finds they have become iron deficient. The unsuspecting or incompletely informed clinician or GP may then order a battery (literally) of investigations and a variety of invasive endoscopies, which put the donor at extra and completely unnecessary hazard. In this way we really have turned the initially happy donor into a most unhappy patient. A basic understanding of iron metabolism and careful history taking can often avoid such unpleasantries.

Furthermore, donation collection sessions are NOT health clinics; indeed the UK Blood Services strenuously avoid activities which may tempt people to donate for reasons other than altruism. Such is the case (which we know happens still) for people who really want to know their HIV status. They avoid answering the specific questions on the (admittedly formidable) donor questionnaire, complete the selection process, give their blood and then have to wait for the no-news; for in this case 'no news is good news' which is obviously most unsatisfactory for the donor. It is even more unsafe for patients as the screening tests may fail to detect markers of recent infection, yet the blood be infectious.

But perhaps the most contentious result of confusing patients with donors, and vice versa, comes when considering issues such as 'Human Rights'. Whereas patients have obvious rights regarding therapy and management, the rights of the public to become donors are more limited. Although those who successfully reach the donor couch have real rights on a par with those of patients, the rights of those who have been deferred – apart from being treated decently – are more restricted. These are mostly that they be given opportunity to receive a frank and full explanation for their deferral. If those reasons have medical implications, they have the right to proper clinical referral, but those whose lifestyle or occupation puts them and any recipients of their blood at demonstrably higher risks do not have the right to give blood.

I must thank all the contributors, especially Sue Armitage who has now contributed to two successive issues of 'Blood Matters'. Those who read both her articles will get a rather more complete insight into the world of stem cells. I must also thank all my co-editors, and Alison Murray, Tim Wallington and also Angela Robinson, who put me up to this.

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Evidence-Based Donor Selection and the European Directive

Just as in clinical practice, the case for basing donor selection criteria on the best evidence available seems self-evident. But this is easier to say than to do. When donors were relatively plentiful it was easy to defer any 'sub-optimally fit' donors; for example those on medication or with a history of conditions such as asthma (even if it was not in season). Principles of fairness and the need to sustain supplies have produced very different attitudes. Donors with controlled medical conditions (such as depression) but who are otherwise fit enough to tolerate the donation process may now give blood if their condition and any medications they take do not adversely affect the quality of any components derived from their donation. This approach requires increased selectivity.

Particularly since HIV was identified in 1983, and more recently in accordance with the European Directive, the UK Blood Services have refined their donor selection criteria considerably, though much more needs to be and is being done. It should be commented that much of the Directive was based on work by transfusion experts within the Council of Europe (CoE) many of whom were British; and although some criteria have impacted on British practices, most were anticipated and their incorporation has, on the whole, been satisfactory. The CoE should not be confused with the European Union: the Council has 45 member nations, from Albania to Ukraine, while the Union now has 25.

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This article will emphasise four aspects – donor haemoglobin levels (Hb), malaria, hypertension, and men who have sex with men (MSM).

Haemoglobin

Rules are required to prevent donation by anaemic or iron deficient donors – for blood quality and for donor health. Prior to 1999 the UK applied the CoE Hb criteria of 125g/l for women and 135g/l for men, determined by an approved method (in UK, copper sulphate gravimetry on a finger-stick blood sample) immediately before each donation. Although developments within the UK indicate that these values may be rather high – especially for men – nevertheless the Directive sustained the CoE rules and since summer 2005 the NBS has applied the 125/135 values. This undoubtedly helps protect the most vulnerable donors (mostly younger women) from the impact of frequent donation on their iron status, although there is a case for further scrutiny of the evidence.

Malaria and other tropical infections

Malaria and other tropical infections have always been problems and are increasing with more global travel. Recent UK and EU policies have been developed on advice from tropical diseases experts. Although the current situation is workable there can be difficulties – such as geographical definitions and, indeed, some donor dissatisfaction. Nevertheless, transfusion transmitted malaria is still very rare in the UK. Fortunately, criteria for other tropical infections such as Chagas' disease (South American trypanosomiasis) are more straightforward as there is good evidence that testing donors who have resided in endemic areas will identify those very few in the UK who may pass on the infection. The problem is more profound in the USA and even in Canada where substantial contributions to the blood supplies are made by Hispanic donors, many having been previous residents in endemic areas of South America.

Hypertension

The routine measurement of BP was abandoned as a mandatory measure by the EU in 2003. Donors referred to their GP for 'hypertension' detected at sessions in the UK often had no abnormality, yet their 'white coat hypertension' recurred at their next attendance! However, for truly hypertensive donors selective measures apply, and those medicated with ACE inhibitors are barred. But this rule needs to be updated to be consistent with the modern management of hypertension. Nevertheless, the evidence shows – perhaps counter-intuitively – that donors with higher BP faint significantly less often.

Men who have sex with men

The evidence for barring MSM from donating blood is soundly based, though frequently (and vocally) contested by those who claim that our policy is unjustified – and even denies human rights – as more heterosexuals than MSM in the UK are now newly diagnosed with HIV each year. However, from HPA data and sociological surveys it can be estimated that approximate numbers of men newly diagnosed with HIV in the UK each year are very approximately

1 in 1000 for MSMs;

1 in 2,000 for men who are not homosexual or bisexual, but who may have other risk factors such as drug use or born overseas (especially in Africa);

1 in 40,000 for heterosexual men with no other identified factor which might put them at higher risk.

We can expect continuing challenges to our policies, including from registered civil partners. Current criteria are consistent with the EU Directive which bars those whose sexual lifestyle puts them at relatively high risk, although occasionally MSM nationals from other EU countries state that they regularly donate at home. The NBS goes by UK epidemiology where higher risk in MSM is amply demonstrable.

Many other issues – such as history of malignancies, age, etc – are frequently discussed. All criteria are regularly examined and re-adjusted whenever possible. However policies have to fit working conditions at sessions, and pragmatism has, occasionally, to modify the 'science'.

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Adverse Events in Whole Blood Donors

In 2005, 1.2 million National Blood Service (NBS) blood donors gave 2.1 million whole blood donations. For the majority this was a worthwhile and problem-free experience, but adverse events did occur. Whilst most were relatively minor, a small number of donors experienced more serious events and required medical care from their GPs or local hospital.

In general, adverse events such as vasovagal reactions which occur during the blood collection session are well documented; but we have to rely on donors to report any events occurring after they leave the session. For example, they may call the National Contact Centre (24hr access to NBS medical support), or make a complaint, or just mention it when next they attend. Any system recording delayed events in such ways will inevitably underestimate the true incidence and type of problems. More accurate data may be collected by post-donation interviews or questionnaires. In one such study of 1000 American donors[1], 37% of donors reported one or more adverse event (bruising 22%, haematoma 2%, sore arm 10%, fatigue 8% and vasovagal reaction 7%).

NBS Donor Adverse Event Reporting

During 2003 the NBS introduced a system for routinely recording all donor related adverse events which occurred during, or were reported following, blood donation. As there are no international definitions or categories, we developed our own.

The results from 2.45 million attendances (April 04 – March '05) are given in Table 1[2].

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Vasovagal events

Of the 33,075 vasovagal events, 85% did not lose consciousness (grade 1). Of those who did suffer syncope two thirds were uncomplicated (grade 2) and the remainder (grade 3) had one or more complications such as incontinence, physical injury or delayed recovery. Of all vasovagal events 71% occurred in women, 34% in new donors and 52% in the age range 17-30 (these younger donors represent only 25% of the donor base). 3% (1057) occurred after the donor had left the session. Of women aged 17 to 20, about 8% had a vasovagal event – mostly mild.

Venepuncture related injuries

These are also carefully defined but, with the exception of arterial puncture, associated complications present after the session and are therefore significantly under-reported. But it is important to capture the donor's information as it enables us to provide appropriate care.

In the same 12 month period, the following were recorded:

64	arterial punctures (1:38000)
155	direct nerve injury (1:16000)
1891	bruise/haematoma of all grades (1:1300)

Serious Adverse Events of Donation

The NBS also keeps more detailed information on any adverse event causing a donor to require clinical care outside the NBS. 498 donors (1:4900) did so in the 12 months to August 2005. Some were relatively trivial but nevertheless alarmed the donor sufficiently to seek medical advice. Half were due to vasovagal problems – e.g. slow recovery or physical injury for which an ambulance might be called. 35% were venepuncture related: sore arm, swelling and/or infection, or persistent neurological symptoms.

We had no reports of those very rare serious complications - such as compartment syndrome, arterio-venous fistula formation and upper extremity DVT - which have been reported elsewhere. Temporal association of potentially fatal events such as stroke and myocardial infarction is extremely rare; there is no evidence that blood donation per se is the cause in otherwise healthy donors.

Table 1
Vasovagal events reported April 2004 – March 2005

	Number	% of total v v events
Total	33075	100
Grade 1	28071	85
Grade 2	2728	8
Grade 3	1210	4
Delayed (all grades)	1057	3

Four donor deaths have been reported in the UK in the last 20 years. These were due to undiagnosed cardiomyopathy (2), head injury (1) and, at inquest, natural causes (1). There have been no deaths reported in the UK since 2001.

Conclusion

The NBS now has a robust system for reporting and recording adverse events in our own donor population. This will permit meaningful comparison with those from other Blood Services and also reliable assessment of any future changes in blood collection protocols e.g. proactive interventions to reduce the number of adverse events.

Minor adverse events following blood donation are relatively common. Whilst serious adverse events are rare, 10 blood donors seek medical advice outside the NBS every week. The CMO's Appropriate Use initiative concentrates on the benefits to recipients of avoiding transfusion. Another driver should be an appreciation that each request for blood translates into another request for blood donations from voluntary donors for whom the risk is not zero.

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Adverse Events in Component Donors

Modern cell separator machines allow flexible collection of tailored components from individual donors. A donor, carefully selected for platelet count and haematocrit, can donate the equivalent of 2 to 3 adult therapeutic doses (ATD) of platelets; i.e. the platelets recovered from 8 to 12 whole blood units. Furthermore, 2 units of red cells, or combinations such as 1 unit of red cells and 1 ATD of platelets, can be collected at a single visit.[1] Modern cell separators are more portable but use the same centrifugation principles, but their portability means that they can be used on blood mobiles and at mobile session venues.

The adverse events that can occur in component donors are (1) those common to whole blood donors - venepuncture related, vasovagal reactions or faints (2) those consequent on the use of cell separators and (3) those relating to the citrate anticoagulant.

Venepuncture related events

These include bruising at the venepuncture site, neurological needle damage, arterial puncture etc. as with whole blood donors, although because the selection criteria for component donation includes good vascular access they occur much less often than in whole blood donors.

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Vasovagal reactions

Vasovagal reactions are much rarer in component donors than whole blood donors as some fluid replacement (saline and anticoagulant) occurs during the procedure on the cell separator machine.

Citrate toxicity

Citrate is the anticoagulant of choice in component donation, for example Acid Citrate Dextrose Formula A (ACD-A.). Citrate acts by binding ionised calcium and this may cause a transient hypocalcaemia which is usually well tolerated in donors. However, decreases in ironised calcium can increase the excitability of nerve cell membranes, allowing spontaneous depolarisation.[2] This translates to occasional perioral and/or peripheral parasthesias in donors. In mild citrate toxicity the perioral tingling may be described in donors as a "metallic taste" in the mouth or as a sensation of the "machine vibrating". Serious or severe citrate toxicity effects include muscle spasms, chest pain and hypotension, and may lead on to cardiac arrhythmias. Moderate citrate toxicity effects fall in between. Recent questionnaire audits have confirmed that many donors experience mild citrate toxicity during component donation. The incidence of severe citrate toxicity (0.03%) is comparable to that of severe faints following whole blood donation, indicating a comparable margin of safety.[3]

Mild citrate toxicity effects can be stopped by slowing the rate of return of anticoagulated blood/plasma to the donor, but giving calcium supplements to donors (as occurs in other parts of the world) is actively discouraged within the NBS. Any donors who repeatedly show signs and/or symptoms of severe citrate toxicity are withdrawn from component donation and returned to the whole blood donor panel.

Machine related problems

Mechanical faults, electrical/electronic faults, and power failure could all occur with the use of cell separator machines, thereby affecting the component donation process being undertaken at the time. There are three main types of adverse events:-

1. **Inability to return red cells to the donor**
   This is rectified by deferring the donor for an appropriate donation interval depending on the amount of red cells that are lost.

2. **Haemolysis of cells in cell separator**
   This occurs very rarely during cell separator procedures and may be due to a machine fault.

3. **Clotting within the extracorporeal circuit**
   This occurs rarely. The usual cause is an operator error where the anticoagulant bag is not properly connected to the disposable set, or due to an inadvertent transposition of anticoagulant and saline bags. When this occurs, it is not possible for the red cells to be returned to the donor and the procedure is usually terminated.

Very rare events

Very rarely, errors occur during the manufacturing of the disposable sets (harness) used in component donation and these may adversely affect the donor by haemolysing the donor cells. The NBS quality systems require these harness incidents to be documented and addressed through our quality procedures. Regular meetings are held with cell separator machine manufacturers to discuss ways of refining and improving the processes.

Component Donation has been proven to be safe. Constant monitoring of any adverse events enables us to ensure the safety of our voluntary altruistic donors and of the blood supply, and also to improve our processes.

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Granulocyte Donation and Adverse Reactions

In the words of the old 'Domestos' TV advert, fresh blood 'kills all known germs'. This comes in useful when newly donated blood is stood at ambient temperature before cooling to 4°C in order to eliminate skin commensals contaminating the collected blood. This is a significant overall contributor to blood safety. Granulocytes are the most important 'effector cells', but viability is mostly lost by 24 hours.

Therapeutic granulocyte concentrate preparations were first developed decades ago, but production difficulties, and effective broad spectrum antibiotics limited their use such that a 1997 Prescribers' Journal article by Provan completely ignored them. However, demand for severely sick and septic neutropenic patients never stopped completely: platelet/granulocyte rich buffy coat preparations were used several times for babies, children and occasional adults throughout the 1980's and 1990's. In 1996 the 'top-and-bottom' blood collecting pack was introduced for producing platelet concentrates from pooled buffy coat. Buffy coats can also yield granulocytes, by adapting the spin-cycles, and can give up to $1x10^9$ granulocytes in about 50ml per donation; 10 units are usually used for treating an adult. This product is not listed in the UK Transfusion Services (JPAC) 'Red Book' and has to be used on a concession basis. It has so many red cells that some recipients have to be venesected. About 3000 donations' worth were issued in the last year – clinical responses are varied and impossible to analyse systematically. The NBS is developing improved methods for optimising granulocyte yield in a multi-donor product which may have better function and cell survival.

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Single-donor granulocyte component production has also become more refined. This is the only granulocyte product listed in the Red Book. Early apheresis methods filtered and eluted the granulocytes from absorption columns; but the cytokines released from degranulation caused severe reactions often resembling TRALI in the recipient and less frequently in the donor. Currently only centrifugal apheresis methods are used and to maximise yields sedimenting agents are added to the circuit such as hydroxyethyl starch, and the donor is premedicated with dexamethasone which demarginates the granulocytes in the donor circulation. The NBS' protocol for apheresis granulocytes from single random donors only yields sufficient granulocytes ($\leq 5x10^9$) for treating younger patients under 30kg. The collection of significantly increased yields has been possible following the premedication of the donor with recombinant growth factors including granulocyte colony stimulating factor (G-CSF). As many as $5.0x10^{10}$ granulocytes, which is equivalent to 50 single donor buffy coats, can be produced from one donor in one sitting but this has raised profound ethical issues.

The main ethical consideration concerns the use of recombinant growth factors and the potential immediate side effects of cytokines, with the uncertainty about the long-term complications of such factors. So using such factors in healthy people is justifiable only exceptionally. Significant side effects are becoming better recognised, such as red cell aplasia in renal dialysis patients receiving recombinant Erythropoietin (Epo). Donors receiving G-CSF suffer side effects far more frequently than donors of any other component. One report claims that 96% experience bone pain, and more than 75% headache, myalgia and malaise. Insomnia, nausea, sweats, chills and anorexia are common, as are reactions at the injection site. In addition, there are anecdotal reports of GCSF-induced thrombocytopenia and concerns about a theoretical risk of leukaemia in the long-term. Serious side effects including posterior subcapsular cataracts have been reported following short term and even single doses of corticosteroids. A Brazilian study of community donors presented at AABB in 2005 claimed a more modest 18% of donors to have 'mild to moderate' reactions to Dexamethasone or G-CSF but this remains a high incidence in comparison with other donors. These potential adverse effects place an even greater obligation on clinicians organising granulocyte collections to advocate the *donor's* interests. For example, it may be that recombinant G-CSF to boost granulocyte yield is only justifiable for family donors or for unrelated donors when part of a controlled clinical trial.

Clinical guidelines for the use of granulocyte transfusions have been produced by the NBS (available on its website) partly to ensure donor safety by limiting use to definite indications. Requests for such products have to be discussed with NBS medical consultants. Following implementation of the European Directive on blood products in November 2005, hospitals can no longer prepare granulocytes from donors, even those from whom they have previously collected stem cells, unless they become a licensed 'Blood Establishment' like the NBS. Granulocytes have to be gamma-irradiated (25 Gy), to render remaining lymphocytes non-proliferative. They should be used as quickly as possible and within 24 hours from collection. It is axiomatic that given the significant presence of red cells, appropriate standard compatibility tests be conducted. For patients with HLA antibodies, granulocyte transfusion may become ineffective or cause TRALI-like symptoms. Therefore, HLA matched products (if available) may be indicated although anti-granulocyte antibodies are very rare and 'cross-matching' is difficult technically; so there has to be a balance of risks when preparing and using such products.

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Blood Donors and Iron Deficiency

In the UK regular whole blood donors donate at a minimum interval of 13 weeks but no more than three times a year. The NBS specification for donation volume is 450 ±45ml of blood, although the NBS target volume - ascertained by careful automated measurement at the donor bedside - is 470ml. About 20ml extra is needed for blood group and microbiology testing so that up to 500ml is taken at each donation – about 240mg of iron from women and 270mg from men. Many Europeans give 500ml rather than 470. In America donors may give every 8 weeks, but on average US donors give between 1.1 and 2.1 times a year. UK donors give 1.3 times a year, but about 15% attend as often as possible – with possible health consequences such as iron deficiency, with or without anaemia.

In the UK, donor Hb is assessed at each attendance by a pass/fail method using copper sulphate solutions of fixed specific gravity (1055 for men, 1053 for women, equating to the European standard Hb of 135 and 125g/l respectively). If an introduced droplet of blood sinks, the donor 'passes'. This method is cheap and easy, which is why it is still used, but is undoubtedly inaccurate as at least 5% of donors are passed and failed inappropriately. So some anaemic donors may give blood although the Hb standard is deliberately set to allow for this. The NBS checks the Hb of failing donors on a venous sample using a portable haemoglobinometer (HemoCue) – about a third turn out to be above threshold.

A healthy person contains 3-5g of iron; about two-thirds is in circulating Hb and 5-20% in storage. In iron deficiency the Hb falls when the stores become exhausted. Men need to absorb 1mg iron from the diet daily, but menstruating women need up to 2mg. Only about 10% of dietary iron is absorbed and although absorption is increased in iron deficiency, women tend to eat less iron, though some buy their own iron supplements.

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For every unit donated a year the donor's daily iron requirement increases by 0.7mg; so daily iron absorption for donors giving 3 times a year needs to be about 3mg for men and 4mg for women. Whereas men donating blood 3 times a year can avoid iron deficiency by eating a good diet, women find it very difficult. It was thought that iron deficiency without anaemia caused no detriment, and indeed that women were protected against ischaemic heart disease by their relatively low iron stores; so men were encouraged to donate because as well as helping others their risk of ischaemic heart disease was thought to be reduced. This is no longer accepted.

Men donating frequently can become iron deficient, though not often anaemic. The mean serum ferritin of 103 men in North London giving an average of 11.5 blood donations during the previous 3 years was 35.3ng/l (normal range 15-300ng/l); it was 15-30ng/l in 31%, indicating low iron stores; and below 15ng/l in 20%, showing virtual absence of iron. The venous blood Hb of all 103 donors was greater than 135g/l using a Coulter analyser. Of 88 of the 103 who were questioned, none were vegetarian although some ate little or no red meat. None had a history suggesting chronic blood loss. In comparison, 31 men prior to their first donation had mean ferritins of 85.4ng/l. Two of the 31 non-donors were vegetarians; in none was the ferritin below 15ng/l, although in 2 (one a vegetarian) it was below 30ng/l.

There is evidence of reduced intellectual capacity in non-anaemic iron deficient people. Children, adolescents and adult females have often been studied, but not males. A joint study from South Africa and the USA in 2003 demonstrated a significant relationship between iron status and cognitive functioning, depression, anxiety and anger, in women with iron deficiency anaemia, and in iron deficient but not anaemic women.

Iron supplementation remains controversial. Perhaps removing so much iron from healthy individuals that they need to take supplements is not justifiable. Iron supplements are not without risk; there can be side effects such as nausea, vomiting, abdominal pain and constipation. They may mask chronic GI haemorrhage and delay the diagnosis of serious disease. Children swallowing iron tablets intended for adults may die. Even if small doses of iron are used, compliance may be a problem.

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Editor's Note
The NBS is exploring practical methods for improved donor assessment in order to anticipate and prevent iron depletion, and to better understand the iron status of our current donors. A variety of additional measures is being considered, such as monitoring the red cell indices and/or serum ferritin measurement in selected donors. Although such initiatives could add significant complexity for donor management and be heavily dependent on sophisticated IT support, session procedures may be simpler. 'Personalising' the donation interval so that individuals donate at a frequency which protects them from iron depletion may be feasible: some may donate more often than 16 weekly while the maximum for others may be just once a year. In the meantime we aim to improve Hb screening before donation, and introduce non-invasive methods when available.

Why Blood Components are Recalled from Hospitals

This article describes recalls of blood and blood components from hospitals by the National Blood Service (NBS) because of possible infection risk, including viral, bacterial and parasitic infection.

A recall may be triggered in two main situations:

- "post-donation information" received from a donor, hospital or GP, indicating the possibility of infection in an individual who has recently donated blood.
- notification of infection in a recipient, where transfusion is thought to be a possible source of the infection. Other components from the potentially infected donor or from the donations that the infected patient received are recalled, as a precaution.

Recalls may take place for other reasons, such as discovery of a problem which could affect the quality or safety of an issued blood component, but these are outside the scope of this article.

Notification of infection in a donor

Because the NBS will only be notified when the donor becomes unwell, and this might be days to weeks after donation, there is a high probability that blood components will already have been transfused. Nevertheless, recall is the first response, as a precautionary measure. The NBS will attempt to obtain as much information as possible about the putative illness in the donor, but at the time of recall an accurate diagnosis may not be available.

- The receiving hospital laboratory(ies) is asked to discard untransfused components.
- Action for transfused components will depend on the nature and certainty of the diagnosis in the donor, but will usually include informing the clinician(s) caring for the recipient(s) of any implicated components.
- Further action may include assessing the susceptibility of the recipient, including testing for specific markers of infection, such as in cases of viral hepatitis A or hepatitis E infection, or the administration of antibiotics, or specific or normal human immunoglobulin, to the recipient.
- Close liaison between NBS staff, including NBS clinicians in Transfusion Microbiology, and the clinician caring for the recipient is essential both to investigate whether transmission of infection has occurred and to ensure treatments are given which may avert or attenuate disease. Prompt action following notification of suspected infection in a donor could be life saving for the recipient.

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- If subsequent information confirms that the donor is suffering from an infection which could be transmitted by transfusion (e.g. hepatitis A), the NBS logs the case as a "predicted" post transfusion infection investigation and collects the information needed to complete a "post transfusion infection surveillance" report. This in turn is incorporated in the annual Serious Hazards of Transfusion (SHOT) report.
- If further information reveals that there is no likelihood of consequences for the recipient(s) of the donation, then this will be passed on to those involved at the hospital, so that the case may be "closed".
- One special situation relates to notification to the NBS of individuals who may have been blood donors and have subsequently developed vCJD. This information is provided routinely by the National CJD Surveillance Unit in Edinburgh to the NBS. Very rarely, a recent donation may be identified from one of these individuals; any in date components will be recalled as a matter of urgency.

Notification of infection in a recipient

- When a blood recipient is reported as having an infection, and there is a possibility that this could have been transmitted by blood transfusion, an investigation of possible transfusion transmitted infection is triggered.
- In the investigation of viral or parasitic infection, a routine check establishes what components were produced from the index (and any subsequent) donations. Hospital laboratories will be notified of any 'in date' components from the involved donors so that untransfused components can be discarded. This action is taken before any further investigation has taken place, and is very much a precautionary measure since transfusion is only rarely shown to be the source of infection in the recipient. If the investigation reveals that the donor has seroconverted for the infection, a recall and lookback into the fate of the last negative donation will be carried out.
- Notification/recall of components for investigation of possible bacterial contamination usually follow the report of a reaction in a recipient, where bacterial contamination is part of the differential diagnosis. Other in date components (usually red cells and FFP, since the index case most often relates to platelets) are recalled as a precaution, but may also be required for investigation. The vast majority of investigations reveal no evidence of bacterial contamination in the index component, so no further action is needed. Where contamination is confirmed, the investigation includes routine follow up of the health of any other recipients of components from the same donation and taking swabs from the donor's arm for bacterial culture for comparison with the organism found in the component. The results of the investigation will be collated and reported to SHOT.

Because blood components move across the country, recalls may be triggered by a blood centre remote from the receiving hospital. Communication is very important, and the NBS is committed to ensuring that hospitals clearly understand who within the NBS should be the point of contact for further information and advice.

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The Problem to the NBS of Microbiologically Reactive Donors and How the NBS Manages Donors with Confirmed Positive Microbiological Markers

Reactive microbiological tests

The majority of microbiologically reactive tests on blood donations are false reactions. This is no reflection on the validity of the tests but an accepted aspect of all biological tests. Each National Blood Service (NBS) testing site sees approximately 5 falsely reactive tests per day, which may be compared with about 2 confirmed positive results per month. Falsely reactive results are of no significance to donors, or their health, but donations giving false reactions cannot be issued. As it is unethical to take donations which cannot be used, these donors must be informed.

Donors are informed by letter and given the telephone number of the NBS National Contact Centre in case of concerns or questions. Calls are referred to medical staff who can give further advice to the donor.

All donor contacts refer to 'reactive' (rather than 'positive') results, and emphasise that the result is of no significance to the donor's health. Specially designed material is available to reassure the donor. The screening test giving the reactive result is not named, thus preventing the donor from asking irrelevant questions about an unsubstantiated infection and being led to believe that he/she is infected. A leaflet explaining the general principles of false reactions, their relative frequency, and the routine nature of management is sent with the letter. Donors are told that samples and not a donation will be taken at the next attendance, in order to avoid wasting a donation. Fortunately, most false reactions are transitory. Following a repeat test most donors can continue to donate after a statutory interval, having resumed their normal negative testing pattern.

Confirmed positive results

In accord with the principle of duty of care, it is NBS practice to notify donors who are confirmed positive for any microbiological marker (with the exception of cytomegalovirus - CMV). Notification is a clinical task and the NBS Consultant for Transfusion Microbiology has ultimate responsibility for the process. Suitably trained medical staff are available at NBS centres to see and speak to these donors.

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Primary notification is by letter. Donors with hepatitis B, C or human T-cell lymphotrophic virus (HTLV) are told which infection they have, and an information leaflet is enclosed. Most donors accept the invitation for a face-to-face interview following the letter, but a discussion may be held over the telephone. Such an interview requires staff who are skilled communicators.

Donors with HIV infection or evidence of syphilis are notified by letter only of an unusual and significant test result. In the case of syphilis, the vast majority of discussions can and do take place over the telephone, prior to direct referral to a GUM clinic. Donors told they have HIV can be very shocked, so are seen in person. It is not possible to offer appropriate support by telephone to a very distressed donor. Donors may be seen at a blood centre, local hospital or at the GP surgery, but never in their own home. The presence of third parties is discouraged unless the donor has already been told about the infection and requests an accompanying person to be present.

The objectives of the discussion with any donor are to:-

- explain the meaning of the results and why further donation is not possible
- confirm results with a further blood sample
- explore the consequences for the donor's future health and circumstances
- arrange appropriate medical referral
- reduce the risk of onward transmission
- obtain information about source of infection (which can be useful for donor selection)
- maintain confidentiality.

The donor's particular concerns may include:-

- future health
- medical referral/investigations/treatment
- transmission to others
- lifestyle changes
- sexual practices
- pregnancy
- employment, finances and insurance
- confidentiality
- whom to tell/concerns about telling partners
- early death/care for dependants
- what the donor will do immediately after leaving the session.

Whenever possible, a second blood sample is obtained, to confirm that the results are consistent and relate to the correct individual. The donor is given the results and referred for specialist medical advice. Informed consent is required before information about donors' test results, medical or risk history is disclosed to any third party (including the GP). On rare occasions, it is necessary to consider disclosure without consent. Such disclosure is made only after appropriate consultation.

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What has Leucodepletion Done for Patients?

When universal leucodepletion (LD) was mandated by the Department of Health in 1998, the drive was to try to reduce what was then considered the theoretical risk of transmission of variant Creutzfeldt-Jakob Disease (vCJD) by blood transfusion. Implementation was completed by November 1999 and since then all blood components have been leucodepleted to less than 5×10^6 leucocytes per unit in 99% of components with 95% statistical confidence. It has long been realised, however, that the incidental presence of leucocytes in blood components can cause problems to transfusion recipients, and therefore leucodepletion may confer beneficial effects other than vCJD risk reduction.

Cytomegalovirus (CMV) is a white cell-associated virus, transmissible by transfusion, which can cause severe infection in susceptible immunocompromised patients. There has been considerable debate over whether LD is an acceptable alternative to CMV serology testing for reducing transfusion-transmitted CMV infection. The American Association of Blood Banks (AABB), the British Committee for Standards in Haematology (BCSH) and Council of Europe guidelines all regard LD as equivalent to testing, although the Joint UK Blood Transfusion Services and National Institute of Biological Standards and Control Professional Advisory Committee (JPAC, the 'Red Book' Committee) and the US Food and Drug Administration do not. Data from numerous trials suggest that following pre-storage LD (NOT bedside filtration), transmission rates of CMV are equivalent to rates achieved using CMV serology testing, although neither method alone is completely safe. A Canadian Consensus Conference concluded that both are effective, neither is perfect, it is not possible to decide whether one is better than the other, and the added benefit of using both together is unknown.[1]

Human T-cell lymphotrophic virus (HTLV) is another cell-associated virus. Some laboratory studies show that the amount of viral load can be reduced by LD, although the virus does not appear to be eliminated. Data from countries which have implemented LD and performed lookback studies suggest that LD confers some reduction in risk. Clinical studies however, would be required in order to provide good evidence about how relevant this reduction is for patients, and these would need to be large and would be difficult to undertake.

Transfusion associated graft versus host disease (TA-GVHD) is caused by transfusion of leucocytes to susceptible immunocompromised patients. It was never envisaged when LD was first implemented that it would have any effect on the incidence of TA-GVHD, as it is recognised that very small numbers of leucocytes can cause this disease. However, there has been only one case of TA-GVHD reported to the Serious Hazards of Transfusion (SHOT) Scheme since the implementation of LD, suggesting that although the risk has not been eliminated it has been significantly reduced.

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Non-haemolytic febrile transfusion reactions (NHFTR) associated with platelet transfusions are thought to be mediated by cytokines released from leucocytes contaminating platelet components. Reactions to red cells are more likely to occur as a result of the development of human leucocyte antigen (HLA) antibodies in recipients. Although most studies on NHFTRs are non-randomised there does appear to be convincing evidence that since the introduction of universal LD, febrile reactions to both platelets and red cells are reduced.[2] In practice for many patients this has removed the need to be "pre-medicated" with steroids and antihistamines prior to platelet transfusion.

A significant management problem for many multi-transfused patients including haematology patients is alloimmunisation to HLA antigens resulting in development of refractoriness to platelet transfusion. A randomised trial (Trial to Reduce Alloimmunisation to Platelets or TRAP study) investigated the effect of LD on the development of alloimmunisation and found a reduction following transfusion of LD units from 45% to 20%.[3] This study was performed in patients with acute myeloid leukaemia and although the immunisation rate was reduced there was found to be no impact on death or remission rate or number of transfusions, but follow-up was short.

The immunomodulatory effects of transfusion have been discussed for many years. There is considerable evidence that transfusion of non-LD blood can result in an increased rate of post-operative infection and this effect is likely to be reduced or even removed following leucodepletion.[4] There is less evidence to suggest that transfusion increases the rate of recurrence of tumours.

The main adverse effect of leucocyte depletion is the loss of up to 10% of the component volume in the filter, which may lead to increased donor exposure for the recipient. Other reported side-effects include rare hypotensive reactions in patients receiving transfusions through bedside filters. This complication seems to have disappeared following implementation of pre-storage rather than bedside LD. In addition a 'red-eye syndrome' was seen in the USA after transfusion of blood filtered by filters from one particular manufacturer. This has not been seen in the UK where this manufacturer's filters are not used.

In summary the implementation of LD has been shown to convey considerable benefit for patients over and above the reduction in vCJD risk for which it was implemented.

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Update on SHOT 2004 – Donor Related Aspects

As this issue of Blood Matters focuses on donors, it is appropriate to look at recent blood safety initiatives with implications for donor selection or management. The first is aimed at reducing the risk of bacterial contamination of blood components, the second at reducing the incidence of transfusion related acute lung injury (TRALI), now the leading cause of transfusion associated mortality and morbidity.

Bacterial Contamination

Bacterial contamination of blood components, particularly platelets, has been highlighted by SHOT. Between 1995 and 2003, 29 cases were reported, and 7 deaths. Criteria for confirmation are:

- No evidence of infection before but evidence after transfusion with no alternative source

and either

- Finding the same infection in the donor

or

- Finding the infectious agent in the transfused component

Twenty-five of these 27 cases and 6 of the 7 deaths were due to contaminated platelets. Most implicated organisms were skin contaminants (*Staph epidermidis* in 9 of the 25).

An NBS study (McDonald et al 2004) showed that diverting the first 20ml of donated blood (containing the skin-plug with organisms) reduced contamination by 47% and improved donor arm cleaning by 57%, so that together there would be a 77% reduction. Diversion pouches are now used for all collections and improved skin cleaning, current in apheresis platelet collections, will be rolled out to whole blood donation. Any issues for supply must be considered, as the new arm cleaning method requires the disinfectant to dry on the skin, adding 30 seconds to the donation process. With over 100 donors attending a busy session this may prolong waiting times significantly, reduce collection, and result in donor dissatisfaction. However, validation studies suggest that the new procedure is acceptable to donors and staff.

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The preliminary SHOT findings are encouraging but not conclusive. In 2004, for the first time, there was no confirmed case of transfusion-transmitted bacterial infection. However one patient developed pyrexia and rigors and S epidermidis was found on the donor's arm and in the transfused platelets, but the same infection was not confirmed by recipient blood culture. In another case, transfusion of platelets contaminated with E coli was averted at the bedside because the pack appeared abnormal, which highlights the importance of inspecting blood components for signs of contamination, i.e. abnormal colour, debris, lack of platelet 'swirling', etc.

Bacterial contamination of red cells is much rarer, as few organisms survive refrigeration. Those reported to SHOT were: Coagulase negative Staphylococcus (1), Staph epidermidis (1), Serratia liquefasciens (1) and Yersinia enterocolitica (1). In the latter, and only fatal, case, the donor subsequently recalled some diarrhoea two weeks previously and the organism was isolated from the archive. Hence, although the donor was fully recovered at the time of donation, a bacteraemia was still present. As Yersinia is carried in donor white cells, it is of interest that no case of bacterial contamination of red cells has been confirmed since 1999 when universal leucodepletion was implemented.

TRALI

Investigating suspected TRALI involves recalling all other components from the index donation which the patient received. Many donors may be involved when multi-transfused patients receive pooled components. Female donors are contacted first, and blood samples obtained for HLA/HNA antibody studies. If a match with a cognate antigen in the patient is obtained, the donor is permanently resigned. This requires sensitivity as knowing that their blood may have caused harm, or even death, can be distressing to a donor.

As HLA antibodies are common (up to 15%) in multiparous women and rare in men, the NBS now selects plasma from males for FFP and for suspending buffy coat derived platelets by gender-marking the pack at collection. A dilemma arises with apheresis platelets as the NBS needs to increase the proportion of apheresis platelet collection (to limit the risk of vCJD transmission), but options for reducing the risk of TRALI from apheresis platelets are limited. Substituting some plasma with platelet additive solution, whilst feasible for buffy-coat derived platelets, cannot yet be applied to apheresis platelets. Removing women from apheresis panels would decimate those panels and demotivate many committed donors. Screening plateletpheresis donors for HLA antibodies is being considered, but HLA antibodies do not necessarily indicate 'dangerous plasma' and donor losses would severely compromise supply, particularly of special matched and/or CMV negative components. These conflicting priorities require assessment against a background of increasing restrictions in donor eligibility. At present, recruitment of apheresis donors is directed to males, but a 'TRALI-safe' apheresis platelet supply is not yet achievable. The alternative strategy of suspending platelets in a 70:30 mix of platelet additive solution:plasma is being evaluated.

There is intense interest throughout the world in the outcome of male-only FFP and this year's SHOT report has been eagerly awaited. Twenty-three cases of suspected TRALI were analysed in 2004, of which 13 were 'highly likely' or 'probable'. FFP was implicated in 6; platelets in 4 (3 buffy coat pools, 1 apheresis); red cells in 2 (1 plasma reduced, 1 in Additive Solution); and whole blood in 1. All 13 were from women with leucocyte antibodies. These findings are encouraging, but more data are needed.

Finally, as always, the most common hazard of transfusion remains 'incorrect blood component transfused' (IBCT). 439 reports were analysed in 2004, a 26% increase from 2003 and accounting for 2 deaths. However it is encouraging to note that ABO incompatible transfusions fell to 23, of which 19 were red cells.

This issue of *Blood Matters* provides a welcome opportunity to highlight the implications for donors of some of the recent initiatives that have improved safety for patients and also to emphasise the duty of safe and appropriate blood use.

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Estimated Risk of HIV, Hepatitis B or Hepatitis C Infection in Blood Transfusions in the UK, 2002 - 2004

The likelihood of acquiring an infection through blood transfusion in the UK is kept low by the double strategy of selecting blood donors from healthy volunteer (unpaid) adults at low risk of blood borne infections, and testing their donated blood for markers of transfusion-transmissible infection (TTI). In 2005 all donations were tested for hepatitis B surface antigen (HBsAg), hepatitis C RNA (and some for HIV RNA); and antibodies to HIV, hepatitis C, syphilis and human t-cell lymphotrophic virus (HTLV). Depending on donor history, some donations were tested for antibodies to hepatitis B core antigen (anti-HBc), malaria and *Trypanosoma cruzi*. Universal leucodepletion (except for granulocyte concentrates) also reduces risks for leucocyte-borne infections, including herpes viruses, HTLV and bacteria such as *Yersinia*. Any donation positive for markers of infection is excluded from the blood supply.

These processes minimise the risk of infection by HIV, hepatitis B and hepatitis C. But very rarely a donation infectious for one of these viruses may be collected, not detected, and enter the blood supply. This can happen when: i) a donation is collected so soon after infection that the markers of infection have not yet

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arisen so cannot be detected (this is the so-called Window Period – 'WP') ii) a donation tests falsely negative, or iii) a donation is issued erroneously due to a processing error (e.g. sampling or labelling error, or fault in reagents or equipment).

In the UK, the Serious Hazards of Transfusion (SHOT) haemovigilance scheme (www.shotuk.org) monitors adverse events in transfusion recipients, including TTI. All suspected TTIs should be reported. Each year a small number are identified and reported; the number of reports is, however, undoubtedly lower than the actual number of TTIs, due to under-reporting and under-diagnosis (e.g. of clinically inapparent infections).

An alternative approach for estimating the burden of transfusion transmitted HIV, hepatitis B and hepatitis C virus is to calculate the estimated risk, or frequency, of infectious donations entering the blood supply. This has been done in the UK by closely considering the circumstances that may cause current donation testing strategies NOT to detect an infectious donation. These calculations are based on the frequency of HIV, hepatitis B and hepatitis C infections amongst individuals selected to donate blood, and also a critical appraisal of the testing processes[1]. It is important to remember that no test can be absolutely reliable.

During 2003 and 2004 the risk of hepatitis B, HIV or hepatitis C infectious donations entering the blood supply in the UK was estimated to be 2.02, 0.19, and 0.03 per million donations respectively (table). Approximately 2.8 million donations are collected each year in the UK. The risk estimates therefore indicate that about 11 donations infectious for hepatitis B and one for HIV entered the blood supply during these 24 months: yet only one transfusion transmitted hepatitis B infection and no transfusion transmitted hepatitis C or HIV infections were reported to SHOT. Some recipients would not have survived their presenting illness, which may account for some of the under-reporting.

The accuracy of these risk estimates depends upon accurate information about testing procedures and infections in blood donors. The true risk of HIV, hepatitis B or hepatitis C infectious donations probably ranges between approximately half to 2-fold the point estimates shown in the table.

New donors generally have higher frequencies of infection than repeat donors and therefore it follows that donation from new donors have a higher estimated risk of transmitting infections to transfusion recipients. However, donations made by repeat donors account for a much larger proportion of the total number of donations collected each year, and thus make a larger contribution to the overall risk. For example, during 2003-2004 the risk of HIV, hepatitis B or hepatitis C virus was three, four and eight times higher in donations from new donors than repeat, but repeat donors made nearly nine times the number of donations. Vigilance for high risk behaviours and for infections in both new and repeat donors is therefore important to minimise transfusion-transmitted infections.

These data indicate that the remaining risk of HIV, hepatitis B and hepatitis C infections mandates the avoidance of non-essential transfusions, even though the risk is very low.

Table:
Estimates of frequency of HIV, HBV and HCV infectious donations issued per million donations and 1 per x million donations after testing in the UK, 2003 – 2004

Risk due to:	HIV	Hepatitis B virus	Hepatitis C virus
Window period donation			
per million	0.17	1.95	0.03
1 per x million	5.87	0.51	31.24
All causes			
All donations			
per million	0.19	2.02	0.03
1 per x million	5.22	0.50	29.03
Donations from new donors			
per million	0.44	6.11	0.15
1 per x million	2.26	0.16	6.79
Donations from repeat donors			
per million	0.16	1.54	0.02
1 per x million	6.16	0.65	46.99

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Reference

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Impact of vCJD on the UK Blood Supply

Although first described less than 10 years ago, following recognition of a "new variant" of Creutzfeldt-Jakob Disease (CJD) by workers at the National CJD Surveillance Unit (Edinburgh), variant CJD (vCJD) has already had a significant impact on the UK blood supply.

The impact of vCJD is in three main areas:

- blood donors
- blood donations
- blood usage.

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1. Impact of vCJD on blood donors

- The introduction of new donor selection criteria designed to reduce the risk of collecting blood from a donor incubating vCJD has reduced the number of available blood donors and donations. The most important of these new criteria is the exclusion of individuals who have received a blood transfusion within the UK since 1980. Preliminary work prior to implementation in April 2004 suggested that the impact would be to reduce the number of available blood donations by between 3 and 6 %, depending on how the rule was applied (only to those with a certain history of transfusion, or also to those with a possible history). Without compensatory recruitment efforts, such a loss would have created severe difficulties in maintaining a blood supply.

- Some decisions in relation to blood safety/risk reduction could lead to disaffected donors, who stop donating even though not affected. An example is the donor notification exercise carried out over summer 2005, when just over 100 donors were notified that they were now considered at risk of vCJD "for public health purposes" because their donations were transfused to a recipient who later developed vCJD. A small number of unaffected donors expressed concerns over this decision and indicated that they were considering whether to continue as a donor in future. There is no evidence that this is a significant problem, but this sort of issue is kept under review.

- There is a potential loss of donors through future initiatives. These include extended donor deferral criteria (such as donors of components transfused to people who subsequently develop vCJD, because of the admittedly remote possibility of cause and effect); and more particularly the introduction of a blood screening test for vCJD. Any screening test will produce a number of reactive results. Whether or not these results are confirmed as truly positive (and confirmation is likely to present challenges, especially when a screening test first becomes available), reactive donations cannot be used. Donors may be unable to continue due to repeat reactive screening tests as it is unacceptable to keep taking donations which cannot be used. Furthermore, donors may not want to be tested, and may decide to stop donating when a test is introduced. There is little evidence to suggest that this will happen, but it remains an unknown.

2. Impact of vCJD on blood donations

- At present, no vCJD screening blood test is available but it is likely that one or more will become available within the next 3 years. The introduction of a screening test *will* inevitably lead to a loss of donations through repeat reactive results (whether or not confirmed). It is far too early to know the rate of repeat reactivity, false positivity and true positivity which might be expected. At present there is no immediate prospect of confirmatory tests or alternative assays which could allow reinstatement of donors with falsely reactive screening tests.

- Prion removal filters are being developed as an approach to reducing the risk of transmission of prions by blood transfusion. Filters would be expected to lead to an increase in red cell (and/or platelet) losses, possibly increasing the number of units of red cells/ platelets needed for a therapeutic dose. This in turn would require increased collection targets, and result in increased donor exposure for recipients.

- Where alternative supplies exist, blood components may be imported from areas of the world with little or no evidence of vCJD, such as happened for FFP for children. Knock-on effects include cost, exposure to other (different) risks presented by a non-UK donor base, and more complicated inventory and prescription procedures.

3. The impact of vCJD on blood usage

- When HIV first became a transfusion issue, blood usage decreased in some areas through increased recipient awareness and demands for alternative strategies. There has been a big push for "better use of blood" over the last 4-5 years, which is now beginning to bear fruit. It is not clear whether this reduction in use is due to a greater awareness of good practice, is a vCJD effect, or is primarily due to cost pressures or other issues (e.g. improved surgical/anaesthetic techniques).

- The cost of blood. Every new intervention has a cost. Any introduction of a further test for blood donations inevitably increases the cost of blood through a direct effect (cost of the test kit and any additional staff) and an indirect effect (cost of wasted donations, cost of additional recruitment efforts to replace lost donations/ donors).

The NBS has used market research and donor surveys in an effort to predict some of the impacts of vCJD on the blood supply. These initiatives, together with modelling of likely future supply and demand, help to inform planning and communications with donors.

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Voluntary Cord Blood Donations

Placental cord blood (CB) is rich in stem cells and a proven alternative to bone marrow or peripheral blood as a source for transplanting to children and adults with life-threatening disorders. Identified as such in 1989 when the first sibling transplant resulted in a successful outcome, it has succeeded in patients with malignancies, bone marrow failure, and inherited and immunological disorders. As CB is collected after the cord is cut, banking the remaining and hitherto unwanted 90ml or so of CB harms neither baby nor mother.

The first public cord blood bank (CBB) was established in the New York Blood Center in 1993. CB can be stored in public banks for unrelated patients, or banked for family use - either for an existing sick child (Reed et al 2003)[1] or in private banks for future 'insurance'. The UK Royal College of Obstetricians does not support private banking and has issued guidance[2] (RCOG Advisory Committee, 2001).

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The NHS Cord Blood Bank (NHSCBB), based in London and part of the NBS, started collecting CB for unrelated use in 1996. It does not bank directed donations requested by families for their own use as this is considered commercial. However, clinicians looking after a family with a child whose disorder could be treated with stem cells may get NBS support for a directed CB collection from a subsequent healthy baby.

Over 180,000 altruistic CB donations have been banked worldwide and 6,000 transplanted. Results compare favourably with bone marrow transplants (Rocha et al 2004)[3]. From 7,800 donations in the NHSCBB, 107 CB units have been transplanted.

As donated adult stem cells must be compatible with the patient, and the leucocytes rigorously matched for tissue type, only about one-third of patients find a matching relative. The remainder require an unrelated donor. Registries must be searched and would-be donors contacted for stem cell harvest. This takes an average of four months so many patients die before a match is found. Often no match is available, particularly for ethnic minority patients. Unrelated CB provides an 'off the shelf' product requiring less stringent matching than bone marrow. After being collected, tested for microbiology, tissue-typed, frozen and stored in liquid nitrogen, a selected CB unit can be issued within 2 weeks – in urgent cases within 24 hours. Maternity units covering ethnically diverse populations can be selected for CB collection, thus compensating for the white Caucasian dominated International Bone Marrow Registries. Approximately 40% of NHSCBB donations are from ethnic minorities.

Effective recruitment is crucial. At the NHSCBB the Bank staff take responsibility for recruitment, but support and collaboration from hospital midwifery and obstetric staff is pivotal. The mothers need information while pregnant with the potential donor; informed consent for collection must be obtained before onset of labour; the collection made and the appropriateness and safety of the donation assessed against donor selection guidelines.

The UK antenatal care 'system' provides a challenge to CB donor recruitment. Mothers with uncomplicated pregnancies generally attend hospital only twice before delivery: at 12 weeks for 'booking' and at 20 weeks for a scan. Most care is given by community midwives and GPs – for a medium sized maternity unit this could involve 85 separate clinics.

At hospitals associated with the NHSCBB, where CB donation is a routine part of the delivery procedure, all mothers receive an information leaflet at their 12 week appointment. Posters are strategically displayed in the hospital and in GP/community midwife clinics feeding the maternity unit. The mother's appointment at 20 weeks includes a letter inviting them to donate their CB, explaining what is required and listing the major exclusions. If they want to donate they complete a card providing contact details. This enables CBB staff to phone them, obtain consent, and start the process of screening out donations which could put potential transplant patients at avoidable risk. The mother receives a consent form to complete and file in her hand-held maternity notes. At delivery consenting mothers are identified and the placenta passed to CBB staff based on the delivery unit to collect the CB. Following collection, the CBB staff visit the mother while still in hospital to ask specific questions on travel and behaviour (such as recent body piercing, which may indicate additional testing), and obtain a blood sample from mother for microbiology testing as for blood donors. Mother is contacted 2 to 3 months later to check her health and that of her baby.

Like our standard donor selection guidelines, those for our CB donors are based on an analysis of risks in transplantation. Indicators are identified by reviewing the medical, travel and behavioural history and by biological testing. The donor interviews are designed to capture evidence of these risk factors through structured questionnaires.

Mothers' responses are very good; over 90% consent to donate. A quote from a mother who has donated cord blood twice - 'It's a fantastic way for my children to start their lives by giving someone else a chance at life.'

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CPD

Objective

After evaluating specific articles published in 'Blood Matters', participants in the CPD Questionnaire should be able to demonstrate an increase in, or affirmation of, their knowledge of Transfusion Medicine.

Credits

Each participant can earn CPD credits, as reflective learning - as designated (or allowed) by the participants scheme (for example 1 credit per hour of reflective study in the RCPath scheme). Each participant should claim only those credits that he or she actually spent in the activity and should write reflective notes in the relevant section of his/her portfolio.

Blood Matters is prepared and issued by the National Blood Service, Reeds Crescent, Watford, Herts WD24 4QN (Telephone 01923 486818)

CPD Questionnaire

Choose the single best answer to the questions below

Q1. In the United Kingdom whole blood donors can give whole blood every:
A. 4 weeks
B. 8 weeks
C. 12 weeks
D. 16 weeks

Q2. A male may give blood if it is estimated that his haemoglobin is greater than:
A. 120 g/l
B. 125 g/l
C. 135 g/l
D. 130 g/l

Q3. A healthy male has a daily iron requirement of:
A. 2 mg
B. 1 mg
C. 3 mg
D. 4 mg

Q4. A standard unit of donated blood contains approximately:
A. 125 mg of Iron
B. 250 mg of Iron
C. 450 mg of Iron
D. 100 mg of Iron

Q5. A menstruating female who donates whole blood three times per annum needs about:
A. 1 mg of Iron per day
B. 2 mg of Iron per day
C. 3.1 mg of Iron per day
D. 4.1 mg of Iron per day

Q6. At the Edgware Clinic in North London, a study showed that in male whole blood donors regularly donating 3-5 times annually:
A. 20% had Ferritin less than 15 ng/ml
B. 6.5% had Ferritin less than 15 ng/ml
C. 31% had Ferritin less than 15 ng/ml
D. 0 had Ferritin less than 15 ng/ml

Q7. Given that there are 2.45 million donor attendances during the period April 04 – March 05 the *reported* Vasovagal events were:
A. 7.35%
B. 1.35%
C. 10.35%
D. 3.35%

Q8. Given that there are 2.45 million donor attendances during the period April 04 – March 05 the *reported* bruise events were:
A. 1.77%
B. 0.77%
C. 0.077%
D. 10.77%

Q9. Given that there are 2.45 million donor attendances during the period April 04 – March 05 the *reported* SAEDs were:
A. 2.0%
B. 0.2%
C. 20.0%
D. 0.02%

Q10. Impact of vCJD on blood donation: preliminary work indicated that exclusion of individuals who have received a blood transfusion within UK since 1980 would reduce the number of available blood donations:

A. between 7 or 10%
B. between 3 or 6%
C. between 1 or 2%
D. 0%

Q11. Universal Leucodepletion:

A. Removes all leucocytes per unit
B. Reduces to less than 1 x 10^6 leucocytes per unit
C. Reduces to less than 0.5 x 10^6 leucocytes per unit
D. Reduces to less than 5 x 10^6 leucocytes per unit

Q12. Universal Leucodepletion:

A. Eliminates risk of CMV
B. Reduces risk of CMV
C. Eliminates risk of HTLV
D. Eliminates risk of TA-GVMD

Q13. Universal Leucodepletion has had:

A. No effect upon incidence of TA-GVMD
B. No effect upon incidence of NHFTR
C. No effect upon incidence of retractonimers to platelet transfusion
D. Some reduction in the incidence of NHFTR

Q14. Microbiologically Reactive Donors: all microbiologically reactive tests on blood donors are:

A. False reactions
B. Due to choice of test systems
C. True positive reaction
D. Confirmed by further testing

Q15. According to 2003/2004 figures there was:

A. 1 case per 5.22 million
B. 1 case per 1.44 million
C. 1 case per 2.11 million
D. 1 case per 6.55 million

] of donations infectious for HIV

Q16. Most implicated organism in bacterially contaminated platelet components was:

A. Serratia liquefasciens
B. Staph epidermidis
C. Yersinia enterocolitica
D. E coli

Q17. Most common hazard of transfusion is:

A. HIV
B. TRALI
C. TA-GVHD
D. Incorrect blood component transfused

Q18. Public Cord Blood Banks:

A. Have been established for less than 5 years
B. Do not exist in the United Kingdom
C. Have fewer than 150,000 donations banked
D. Have used 6,000 donations in transplants

Q19. Granulocyte donations from Buffy Coats

A. About 200 donations worth were issued last year
B. Are not available in the United Kingdom
C. Contain up to 1x10^9 granulocytes in a 50ml donation
D. Contain very little red cell contamination.

Q20. Granulocyte donations from a single random donor by apheresis yields sufficient granulocytes for

A. All adults requiring granulocytes
B. Treating younger patients under 30kg
C. Treating younger patients under 50 kg
D. Treating all patients under 70kg