SERIOUS HAZARDS OF TRANSFUSION **SHOT**

ANNUAL REPORT 2006

Affiliated to the Royal College of Pathologists

The Steering Group comprises members representing the following professional bodies

British Blood Transfusion Society, British Society for Haematology

Faculty of Public Health Medicine, Institute of Biomedical Science

NHS Confederation, Health Protection Agency Centre for Infections

Royal College of Anaesthetists, Royal College of Nursing

Royal College of Obstetricians and Gynaecologists

Royal College of Paediatrics and Child Health, Royal College of Surgeons

Royal College of Physicians, the four UK Blood Services

Published 20th November, 2007

by

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ISBN 0 9532 789 9 9

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1. Foreword: The Future of Haemovigilance in the UK

This is the 10th SHOT Annual Report, completing a decade of haemovigilance in the UK. SHOT was one of the first haemovigilance systems and it has remained the international 'gold standard'. SHOT methodologies have been used to inform and influence the development of systems across Europe and most recently in the USA. This SHOT Annual Report, together with the preceding nine, provides a detailed analysis of data with clinical and laboratory recommendations to improve patient safety.

SHOT data have a high impact factor and are cited regularly in the literature and in National guidelines, Health Service circulars and Department of Health (DH) communications. SHOT recommendations have been quoted worldwide in educational, training, scientific and professional meetings at all levels and in many disciplines. The data have informed DH and UK Blood Services policy decisions regarding blood safety, e.g. in the prevention of TRALI, the leading cause of transfusion-related mortality and morbidity (see chapter 9) and the introduction of measures to reduce bacterial contamination of components (see chapter 12). SHOT has been commended by the Chief Medical Officer (CMO) of England and has supported and informed many aspects of the CMOs' 'Better Blood Transfusion' initiative. SHOT findings were also the basis of the National Patient Safety Agency (NPSA) safer practice notice 14, 'Right Blood, Right Patient', on reducing clinical transfusion errors[1]. In this report, three evidence-based 'Recommendations of the Year' are presented focusing attention on areas where action should be prioritised to improve patient safety (chapter 4).

To build on a decade of success, SHOT is now making a number of decisions about its future plans. This is particularly because of recent far reaching changes in the field of haemovigilance brought about by the European Directives on Blood Safety and the Blood Safety and Quality Regulations (BSQR) in the UK [2,3]. SHOT will maintain its ability to provide leadership in this new era of regulation and biovigilance, and several developments are under way. SHOT's main asset is its extensive data set, which consists of ten years of immensely detailed laboratory and clinical data. In order to utilise the data fully, providing analysis and reporting that is commensurate with the needs of the organisation and its partners, it must be possible to interrogate all the data in a single database. It is anticipated that funding will become available for this development during the current financial year. New reporting categories are to be piloted in the near future, and subdivisions of Incorrect Blood Component Transfused (IBCT) will start in 2008 (see chapter 2).

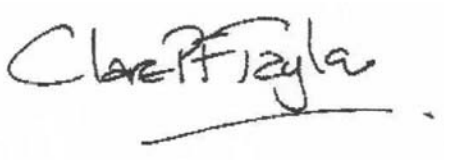
There have been two key new appointments during 2007: a new National Medical Co-ordinator (Clare Taylor) and a new Transfusion Liaison Practitioner (Tony Davies) The new National Medical Co-ordinator is to become Secretary of the European Haemovigilance Network (EHN) and thus will be a member of the Executive Board of the EHN. UK haemovigilance professionals will therefore be able to participate in standardisation of definitions and handling of data in Europe and also internationally through liaison with the International Society of Blood Transfusion (ISBT).

Strategic development of SHOT and UK haemovigilance

SHOT will continue to provide an expert UK-wide haemovigilance service that encompasses not just collection of numbers of events and overall analysis, but the feedback of data and recommendations to all stakeholders and special interest groups to improve patient safety. This will involve SHOT working closely in partnership with the existing regulators at MHRA (the Medicines and Healthcare products Regulatory Agency) who may be co-opted into a new regulatory authority, RATE (Regulatory Authority for Tissues & Embryos).

As the current Competent Authority (CA), MHRA readily acknowledges that its role is as a collector of statistics to fulfil its statutory function, and that all analysis and feedback to users and professional bodies for improving practice and patient safety should come from SHOT, MHRA, through its Blood Consultative Committee (BCC) in January 2007, stated that SHOT 'has a scope of interests that extend into professional and clinical areas beyond the scope of the Blood Directive/Regulations', and added that 'the MHRA is keen to continue to co-operate with SHOT and any other organisations with an interest in haemovigilance.' Minutes of the BCC are available on the MHRA website (www.mhra.gov.uk).

SHOT data will continue to be used to inform policy by the DH, the four UK blood services, the NPSA and the Committee for Safety of Blood, Tissues and Organs. Since its first report, SHOT has advised of the need for this committee, and it is therefore pleasing to see a new development in this area. The committee, until recently called the Advisory Committee on Microbiological Safety of Blood Tissues and Organs (MSBTO), is to be replaced by a new committee entitled the Advisory Committee on Safety of Blood Tissues and Organs (ACSBTO). The chair and members of the new committee are being selected by the Appointments Commission, following advertisement and interview for a number of positions with specified areas of expertise. The new committee will have a wider remit, encompassing all aspects of safety of blood, tissue and organs and also microbiological safety of gametes and human embryonic stem cells. SHOT has made a very significant impact on patient safety over the years, by collecting, analysing and trending data, and looks forward to continuing to support the work of the new committee.



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2. Introduction

SHOT is concerned about the 13% reduction in reports during 2006. It is hoped that this is a temporary effect of the implementation of the BSQR, taking some of the momentum out of SHOT reporting, which hitherto has increased year by year. There is a professional requirement to report to SHOT, as well as reporting being essential for CPA. In order to obtain the maximum impact on patient safety, it is imperative that all eligible reports are sent for analysis, so that a complete picture of transfusion adverse incidents can be analysed. For these reasons, and in response to requests for clarification, SHOT is taking this opportunity to give the following specific advice for users regarding reporting:

- current reporting categories, their definitions and what to report in each category (table 1)
- subdivisions of IBCT
- new reporting categories for 2008
- pilot reporting categories planned
- additional reporting to MHRA
- the relationship between SHOT, MHRA and SABRE

Current reporting categories

These are shown in the accompanying table 1. Each reporting category is shown with its definition (also at the start of each chapter) and there is also a list of the kind of events or reactions required in each category. Readers may wish to cross-reference to the Minimum Standards for Investigation of Transfusion-Related Adverse Reactions, which was developed by SHOT and endorsed by the British Committee for Standards in Haematology (BSCH) Transfusion Task Force (TTF). This can be found in the toolkit on the SHOT website[4]. The IBCT chapter has always contained all reports where error has been a major contributing factor in the case – however there are a number of subcategories that are shown as separate points in the table.

Table 1
Current Reporting Categories

This table shows the active categories for reporting during 2008. Note that isolated febrile reactions and minor allergic reactions have been reported to SHOT this year via SABRE as they are required to be reported to MHRA under the BSQR.

Term	Definition	What to report
IBCT **(Incorrect or Inappropriate Blood Component Transfused)**	All reported episodes where a patient was transfused with a blood component or plasma product that did not meet the appropriate requirements or that was intended for another patient.	This category currently includes: 'Wrong blood' events where a patient received a blood component intended for a different patient, or of an incorrect group, including components of an incorrect group given to BMT/SCT or solid organ transplant patients. Transfusion of blood of inappropriate specification or that did not meet the patient's special requirements. Inappropriate or unnecessary transfusions. 'Unsafe' transfusion where there were handling or storage errors.
Near Miss Events	Any event which, if undetected, could result in the determination of a wrong blood group, or issue, collection or administration of an incorrect, inappropriate or unsuitable component, but which was recognised before transfusion took place.	There will be a new pilot in 2008 and a questionnaire with suitable categories will be developed. It is of note that a large number of events reported to SABRE as SAEs are in fact Near Misses as no component is transfused.
Acute Transfusion Reaction	Reactions occurring at any time up to 24 hours following a transfusion of blood or components, excluding cases of acute reactions due to incorrect component being transfused, haemolytic reactions, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO) or those due to bacterial contamination of the component.	These include: Isolated febrile – rise in temperature >1^{0}C +/- minor rigors and chills. Minor allergic – skin +/- rash Anaphylactic/anaphylactoid – Hypotension with one or more of: urticaria, rash, dyspnoea, angioedema, stridor, wheeze, pruritus, within 24 hrs of transfusion. Severe allergic reaction – Severe allergic reaction with risk to life occurring within 24 hours of transfusion, characterised by bronchospasm causing hypoxia, or angioedema causing respiratory distress. Hypotension – a drop in systolic and/or diastolic pressure of >30mm Hg occurring within one hour of completing transfusion, provided all other adverse reactions have been excluded together with underlying conditions that could explain hypotension. Febrile with other symptoms/signs – rise in temperature >1^{0}C, with no features of an allergic reaction, but with one or more of myalgia, nausea, change in blood pressure or hypoxia.
Haemolytic Transfusion Reaction: **Acute**	Acute HTRs are defined as fever and other symptoms/signs of haemolysis within 24 hours of transfusion; confirmed by a fall in Hb, rise in LDH, positive DAT and positive crossmatch.	Cases with relevant features (see definition) should be reported together with results of all laboratory investigations and antibody identification results if available.

Haemolytic Transfusion Reaction: **Delayed**	Delayed HTRs are defined as fever and other symptoms/signs of haemolysis more than 24 hours after transfusion; confirmed by one or more of: a fall in Hb or failure of increment, rise in bilirubin, positive DAT and positive crossmatch not detectable pre-transfusion. Simple serological reactions (development of antibody without pos DAT or evidence of haemolysis) are excluded.	Cases with relevant features (see definition) should be reported together with results of all laboratory investigations and antibody identification results if available. Cases will be included with no clinical or laboratory features as long as DAT is positive.
TRALI	Acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within six hours of transfusion, not due to circulatory overload or other likely cause.	Suspected cases should be discussed with a Blood Service Consultant, and reported if there is a high index of suspicion, even if serological investigation is inconclusive.
Post-transfusion purpura	Thrombocytopenia arising 5-12 days following transfusion of red cells associated with the presence in the patient of alloantibodies directed against the HPA (Human Platelet Antigen) systems.	Cases where the platelet count drops more than 50% following transfusion should be investigated and reported if complete or partial serological evidence is available.
Transfusion-Associated Graft-versus-Host Disease	Characterised by fever, rash, liver dysfunction, diarrhoea, pancytopenia and bone marrow hypoplasia occurring less than 30 days after transfusion. The condition is due to engraftment and clonal expansion of viable donor lymphocytes in a susceptible host.	All cases where diagnosis is supported by skin/bone marrow biopsy appearance or confirmed by the identification of donor-derived cells, chromosomes or DNA in the patient's blood and/or affected tissues. Cases with very high index of clinical suspicion.
Transfusion-Transmitted Infections	Included as a TTI if, following investigation, the recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection. Plus either at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection. Or at least one component received by the infected recipient was shown to contain the agent of infection.	Cases of bacterial transmission from blood components, where cultures form the patient's blood match cultures from the component bag and/or from the donor. Transmissions of viruses, whether routinely tested for by the blood services or not. Transmissions of other agents such as prions, protozoa and filaria.
Anti-D events	Events relating to administration of anti-D immunoglobulin.	Reports in this section include: Omission or late administration. Anti-D given to a D pos patient or a patient with immune anti-D. Anti-D given to mother of D neg infant. Anti-D given to wrong patient. Incorrect dose given. Anti-D given that was expired or out of temperature control.
TACO (Transfusion-Associated Circulatory Overload)	Any 4 of the following occurring within 6 hours of transfusion: Acute respiratory distress Tachycardia. Increased blood pressure. Acute or worsening pulmonary oedema. Evidence of positive fluid balance.	

New developments in SHOT reporting categories

There have been some shifts in the proportions of different kinds of report, their relative importance in terms of patient safety, and the nature of the recommendations being made. One of the areas most affected is IBCT, which now accounts for three quarters of reports to SHOT. This is discussed below, together with outlines of other new categories for reporting.

IBCT

In 1996/97, IBCT accounted for 47% of reports, and all the reports were around sampling and request errors, laboratory errors, and blood collection and administration errors. After 10 years of evolution, in the 2006 report IBCT accounts for 75% of reports, and almost 50% of cases in this category are not strictly speaking relating to 'incorrect blood component transfused' but to correct blood components being given incorrectly, or handled incorrectly. These changes have often been reporter led, in that incident reports have been sent often without SHOT specifically requesting that category of event. Cases have been sent in by concerned reporters, and, because of the potential impact and learning points, included in the data. In addition anti-D related errors (and omissions) are also included in this chapter, and the numbers have increased as SHOT has actively sought such reports.

With additional staff and new IT, SHOT will be in a position to respond to the changing pattern of reporting and to analyse the data in a way that reflects this and utilises the enormous wealth of information to the full.

In future the 'error' section of the SHOT report will be divided into its constituent parts, without losing the common theme of human error, and new questionnaires will be developed to capture the data from these extremely important categories. SHOT will be explicitly requesting reports on inappropriate use of blood components where patient harm has resulted, as well as giving consideration to collecting cases where harm has resulted from non-transfusion. Anti-D reports will continue to be specifically requested and will be reported as a separate and critically important category. Errors relating to handling and storage of components prior to transfusion are being reported more since implementation of the BSQR[3], where much emphasis has been placed on this – and again these will be reported as a separate category.

Some specific areas of development are:

Anti-D

Anti-D reporting should continue: all errors, omissions and incorrect administration of anti-D should be reported to SHOT. In future this will be analysed separately and form a new chapter of the SHOT Report. Anti-D problems are not reportable to MHRA via SABRE as anti-D is a batched pharmaceutical product. Adverse reactions are reportable to MHRA under their medicines section.

Near Miss

In 2008 SHOT plans to pilot Near Miss reporting, which will be focused in the first instance entirely on sample errors that do not reach the testing phase in the laboratory. A new questionnaire will be designed and circulated to a cohort of hospitals in time for a reporting pilot in early 2008. It will be of great interest to evaluate whether there is a correlation between wrongly labelled tubes and wrong blood in tube episodes, and whether allowing clinical personnel to re-label tubes where there have been mistakes is an unsafe practice. Depending on the outcome of this pilot the categories may be broadened over subsequent reporting years to include Near Misses from other clinical areas. It is of note that a number of the categories that are already being reported to SABRE for MHRA are in fact Near Miss. For any report to qualify as a full SHOT report there has to be transfusion of a blood component to a patient, whether or not there is a reaction. In the Serious Adverse Event (SAE) categories, which are reportable to MHRA via SABRE, many of the SAEs do not result in a transfusion to a patient. Predominantly these are laboratory related SAEs, with some relating to distribution and storage of components elsewhere within hospitals. These are classified as Near Miss in the SHOT reporting structure. For complete reporting in this category SHOT therefore needs to focus on collection of clinical Near Miss events.

TACO

From 2008, reports of Transfusion-Associated Circulatory Overload (TACO) will be collected separately and not as a subset of ATR, where TACO was previously a subcategory. A questionnaire will be specifically designed for this and will be launched in the new reporting year. At the moment a few reports are sent in this category and they have been included variously in the TRALI chapter, the ATR chapter or even under IBCT if an error was involved. The definition of TACO is shown in table 1.

Cell salvage

A new subgroup has recently started to work with SHOT to develop a reporting questionnaire for adverse incidents relating to cell salvage. There will be further updates on progress with this in the SHOT newsletters.

Inappropriate or unnecessary transfusion

There has been an increased number of reports of inappropriate transfusion this year and as discussed above these are currently included in the IBCT category. However, in the future (2008 reporting year) SHOT plans to separate out the inappropriate transfusion adverse events and analyse these separately. Although a small group at present, these incidents are probably under-reported as SHOT has not previously specifically requested this kind of report. Those that have been reported include the two fatalities from the 2006 reporting year, making this a highly significant category for SHOT to develop and analyse to improve patient safety in the future.

Alongside inappropriate or unnecessary transfusion, there is an emerging concern regarding patient harm from under transfusion or non-transfusion. Further developments regarding collection of events in this category will be available in SHOT newsletters and via the website.

Devices reporting

Reporters should remember that any adverse incidents relating to reagents, equipment or other devices used in the hospital transfusion laboratory or in clinical areas may be reportable through the Devices section of the MHRA website, either instead of, or in addition to, the SABRE website. At the moment some reports that have gone to SABRE have been referred to the Devices team at MHRA. Where reporters have any doubts about whether to report to Devices or not, the SABRE helpdesk or a member of the Devices team are very happy to help. All the telephone numbers are available on the MHRA website. A full SHOT report should be filed for devices-related incidents if a blood component was transfused to the patient. Other devices-related incidents may be reportable as Near Miss. Adverse incidents relating to laboratory or hospital computer systems are reportable as usual to SABRE and SHOT, as the IT system is not a medical device.

Medicines reporting

Reports of adverse events or incidents (including side effects) relating to batched pharmaceutical components should be reported to the Medicines section of MHRA. This will include reports relating to Octaplas™, Anti-D, IVIg and other fractionated products. SHOT actively collects all adverse event reports on Octaplas™ and Anti-D, and if they are also reported to SABRE the team at MHRA will ensure that they reach the medicines department if appropriate.

SHOT, MHRA and SABRE

The SABRE (Serious Adverse Blood Reactions and Events) website has now been collecting data for both MHRA and SHOT since November 2005. This SHOT Annual Report 2006 is therefore the first for which notifications have all been via the SABRE site, and the SHOT questionnaires have been completed and sent electronically. Despite some initial technical problems this is an advance that has been welcomed by reporters, and by the SHOT team. Plans are in progress to upgrade the SHOT database and IT software to allow queries, analysis of reports and collation of data to be performed electronically instead of manually.

The two parts of the SABRE website collect data for different reasons. The data collected by MHRA is for regulatory purposes only and a report detailing the numbers of adverse incidents is submitted to the European Commission on an annual basis, using the format and categories in the annex of the EUD amendment[5]. The first deadline for mandatory adverse incidents reporting to the European Commission is June 2008. When adverse events are reported that appear to put patients at significant risk, either by the serious nature of the event, or because of the frequency of occurrence, these are referred to the MHRA inspectorate for further consideration. During the course of 2006 there were no individual SABRE reports that resulted in a visit from the MHRA inspectors to a hospital site. However, whenever the inspection team go to a site they familiarise themselves with any SABRE reports that have been made from that site before the visit.

The data collected by the MHRA is less detailed than that collected by SHOT and places greater emphasis on the section requiring an account of corrective and preventative actions. This section must be completed to the satisfaction of the SABRE team and the inspectorate (if it has been referred) before the case can be closed. SHOT continues to collect very detailed accounts of adverse incidents from hospitals across the UK. This allows for in-depth analysis by a panel of experts for each reporting category, with identification of patterns and trends, and subsequent formulation of recommendations that are initially published in the SHOT Annual Report. SHOT collects incidents occurring anywhere in the transfusion chain, including clinical incidents where there is no involvement of the Hospital Transfusion Laboratory. Entirely clinical based incidents are not collected by MHRA unless transfusion of the component results in the patient suffering a reaction. The new legislation does not require reporting of 'no harm' events occurring in the clinical arena, whereas for SHOT these are a very important and significant category for analysis.

In a full SHOT report the event involves the transfusion of a component to a patient, whereas a SHOT Near Miss is any reportable incident where transfusion did not ultimately take place. Many reports sent to MHRA in the Serious Adverse Event (SAE) category do not culminate in transfusion of a component, as the problem is detected before the component reaches the patient. Thus many reports in the SAE section are classified as Near Miss using SHOT definitions. The collaboration with MHRA through SABRE has therefore provided SHOT with Near Miss data from laboratory-related incidents. In the near future SHOT will be piloting a new Near Miss data collection scheme for clinical Near Misses.

There has been a 13% reduction in the total number of reports submitted to SHOT since the SABRE system came into use. This in particular affects the category of Incorrect Blood Component Transfused (17% fewer cases). It is likely that this is because reporters have been particularly focused on reporting events required under the new legislation, thus reporting fewer clinical IBCT, while there has been an increase in ATR reports. SHOT is hoping that the downward trend will be reversed in 2008 now that the SABRE system has become familiar, and there is more clarity regarding how the SABRE reports are utilised by MHRA.

3. Summary of main findings and cumulative results

This year's report analyses data collected between 1st January 2006 and 31st December 2006

Participation

It has not been possible this year, owing to changes in the reporting system, to calculate the number of individual hospitals submitting reports included in this SHOT report. In previous years, hospitals submitted paper reports to the SHOT office, which were counted and logged manually. Following the introduction of the SABRE electronic reporting system, reporters are able to register with the scheme as either Trusts or individual hospitals. Where Trusts have registered it is not always possible to tell from the information in SABRE precisely in which hospital within the Trust incidents are occurring. From data entered into SABRE and analysed by MHRA, there are 311 registered reporters to SABRE. There are no known hospitals or Trusts that have not registered. From these registrants, a total of 870 reports were submitted to SABRE during 2006, and all relevant reports have been shared with SHOT. There are a handful of registered (i.e. participating) SABRE reporters who did not send reports to MHRA through SABRE in 2006. In addition there were 567 SHOT only reports. Full reconciliation of participation and reporting rates for SHOT and MHRA reports has not yet been possible, but it is clear that mandatory reporting via SABRE has increased overall participation in haemovigilance in the UK, even though the number of reports submitted in SHOT categories is reduced.

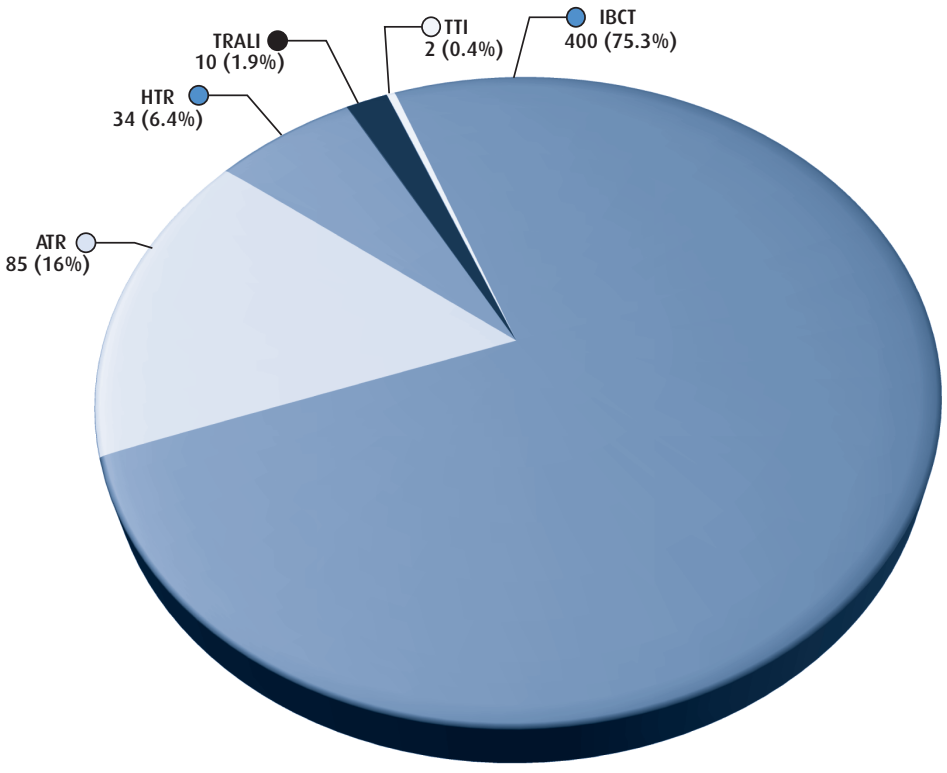
Numbers of questionnaires completed

The total numbers of reports analysed has fallen from 609 last year to 531 this year, a reduction of 13% in total. Table 2 gives a breakdown of reports and figure 1 gives a proportional perspective.

Table 2
Summary of reports reviewed

IBCT	ATR	HTR	PTP	TA-GvHD	TRALI	TTI	Totals
400	85	34	0	0	10	2	531

Figure 1



Numbers of components issued

Table 3
Total issues of blood components from the Transfusion Services of the UK in the financial year 2005/2006

Red cells	2,316,152
Platelets	259,654
Fresh frozen plasma	320,852
Cryoprecipitate	106,139
TOTAL	3,002,797

Overview of 2006 results

Transfusion-related mortality

There were 4 deaths definitely attributable to transfusion reported to SHOT in 2006. Two occurred as a result of incorrect prescribing, in both cases by junior hospital doctors, and these are reported in the IBCT chapter. The first involves lack of precision, and probably knowledge, of component prescriptions for a baby; the second involves a lack of clinical evaluation of a patient with an alleged Hb of 3.9 g/dL. On account of these cases and the large number of reports in which junior hospital doctors contributed to or caused an adverse event, medical education is the theme of the Key Message and main Recommendations this year. There was one death from transfusion of platelets contaminated with *Klebsiella pneumoniae* and one death from TRALI (with imputability 2). Other deaths related to transfusion in 2006 have a lower imputability, but transfusion may have contributed. These related to IBCT, HTR and TRALI and are discussed in the relevant chapters.

Incorrect blood component transfused

There were 400 events analysed for 2006, which represents a decrease of 17% since last year. More direct comparison allowing for the decrease in component usage during the reporting period, and excluding anti-D reports, shows 10.6 reports per 100,000 components transfused in 2006, compared with 12.8 in 2005.

The cases were separated into 7 subcategories as shown below in table 5. In each category the proportion of errors occurring in the hospital transfusion laboratory was calculated: 46% of wrong blood events originated in the laboratory, and 35% of all IBCT.

Table 5
Types of IBCT events

Type of event	Number (%)
'Wrong blood' events where a patient received a blood component intended for a different patient or of an incorrect group	54 (14%)
Other pre-transfusion testing errors (excluding erroneous Hb)	28 (7%)
Blood of the incorrect group given to recipients of ABO or D mismatched PBSC, bone marrow or solid organ transplant	8 (2%)
Transfusion of blood of inappropriate specification or that did not meet the patient's special requirements	108 (27%)
Inappropriate or unnecessary transfusions	51 (13%)
'Unsafe' transfusion where there were handling or storage errors	74 (19%)
Events relating to administration of anti-D immunoglobulin	77 (19%)
Total	**400**

An infant died after rapid transfusion of an inappropriately large volume of platelets, and an elderly woman died after a high volume rapid transfusion based on an erroneous Hb. On further analysis a total of 125 cases, including the two deaths, were found to be due to errors made by junior hospital doctors. This is further discussed in the Key Message and Recommendations of the Year.

There were no deaths related to ABO incompatible transfusion, but two patients suffered major morbidity.

Near Miss events

The SABRE web reporting site was not used in 2006 to collect this data. Near Miss events were collected by the completion of a survey spread sheet. A total of 126 participants returned spreadsheets giving data obtained from 136 hospitals (34.3% return). There was a total of 2702 events of which 1,342 (49.6%) related to sampling.

Next year there will be a further pilot of Near Miss data collection focusing in the first instance on sampling errors.

Transfusion-related acute lung injury

Twelve case reports of suspected TRALI were received in this reporting year, of which two were subsequently withdrawn. Of the 10 cases analysed, two patients died (imputabilities 2 and 0), 7 suffered short-term major morbidity with full recovery and one had long-term morbidity. There were no cases this year related to warfarin reversal. Relevant donor leucocyte antibodies (i.e. donor HLA or granulocyte antibody corresponding with patient antigen) were found in 3 of 7 complete case investigations this year. The reduction in TRALI this year, with the lowest reported mortality since SHOT began reporting in 1996, is likely to be related to the change to preferential use of male plasma.

Other immune complications

There were 85 reported cases of acute transfusion reactions, a 25% increase on 2005, which may be due to the requirement to report all transfusion reactions under the new legislation of the BSQR. These consisted of 20 isolated febrile, 10 minor allergic, 41 anaphylactoid/anaphylactic/severe allergic, 8 febrile with other symptoms, 3 transfusion-associated circulatory overload (TACO) and 3 hypotension. TACO will be requested as a separate category in future. There were no deaths, but 4 cases of major morbidity.

Thirty-four haemolytic transfusion reactions were reported, 11 acute and 23 delayed. There was one death in the acute group probably unrelated to the transfusion reaction, and two cases of haemolysis related to incompatible platelet transfusion. There were no reports of mortality or major morbidity in the delayed group.

In 2006 there were no cases of post-transfusion purpura (PTP), transfusion-associated graft-versus-host disease (TA-GvHD) or events associated with autologous blood transfusion.

Transfusion-Transmitted Infections

During the reporting year, 29 reports of suspected transfusion-transmitted infection were made from throughout the UK to the NBS/HPA Centre for Infection Surveillance. Two reports were deemed to be TTI, both cases due to bacterial contamination of platelets. A report was received in early 2007 of vCJD in a recipient of blood transfusion. This is the fourth case, and involves the same donor as the third case reported in the 2005 SHOT report.

Cumulative data 1996 – 2006

Figure 2
Numbers of cases reviewed (n=3770)
*Formerly DTR

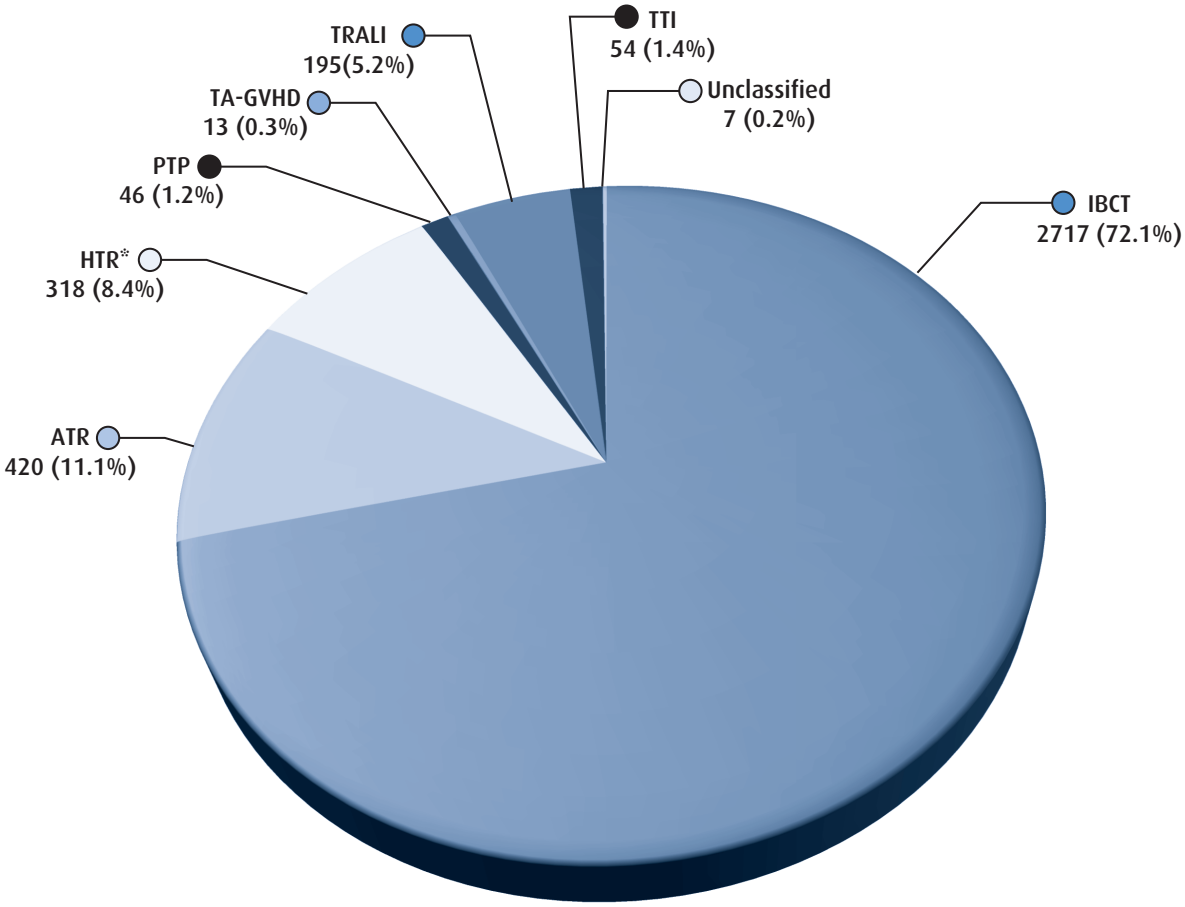


Figure 3
Comparison of report types 1996 – 2006

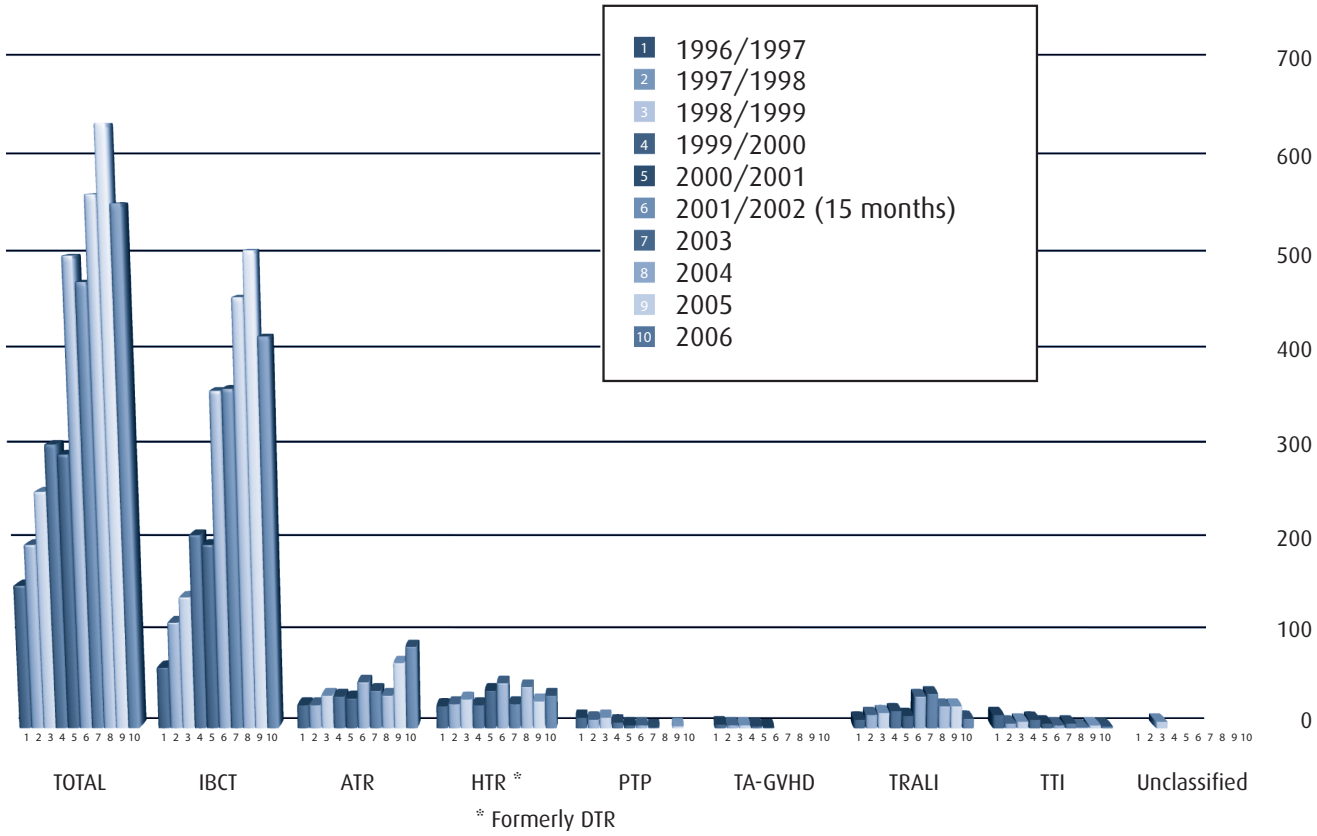


Table 4
Cumulative mortality / morbidity data 1996 – 2006

	Total	IBCT	ATR	HTR*	PTP	TA-GVHD	TRALI	TTI
Death definitely attributed to transfusion (imputability 3)	47	7	2	6	1	13	8	10
Death probably attributed to transfusion (imputability 2)	15	4	4	1	0	0	6	0
Death possibly attributed to transfusion (imputability 1)	47	13	7	1	1	0	25	0
Subtotal 1	**109**	**24**	**13**	**8**	**2**	**13**	**39**	**10**
Major morbidity** probably or definitely attributed to transfusion reaction (imputability 2/3)	315	100	17	29	13	0	118	38
Minor or no morbidity as a result of transfusion reaction	3324	2582	387	280	31	0	38	6
Subtotal 2	**3639**	**2682**	**404**	**309**	**44**	**0**	**156**	**44**
Outcome unknown	15	11	3	1	0	0	0	0
TOTAL***	**3763**	**2717**	**420**	**318**	**46**	**13**	**195**	**54**

* Formerly DTR

** Major morbidity is classified as the presence of one or more of the following:

- Intensive care admission and/or ventilation
- Dialysis and/or renal impairment
- Major haemorrhage from transfusion-induced coagulopathy
- Intravascular haemolysis
- Potential risk of D sensitisation in a female of childbearing potential

*** Excludes 7 cases from 1998/99 that were not classified

KEY MESSAGE

Of the four deaths certainly arising from complications of transfusion in this year's SHOT report, two were the result of error. However, in these cases this was not a single, specific error with direct cause and effect, but a more complex set of circumstances to do with the process of evaluation and decision making, communication with colleagues, and competency and knowledge levels. In each case, any of the personnel associated might have prevented the tragedy had they paused and engaged fully with the clinical scenario. In each case, awareness of and compliance with local clinical and laboratory protocols might also have avoided the outcome. More detailed learning points from these cases can be found in chapter 5, IBCT.

Case 1 – lack of care and accuracy in paediatric prescribing results in over transfusion

A very sick preterm infant, aged 12 months, with multiple congenital abnormalities, had been in hospital since birth and was scheduled for elective surgery. The platelet count was $48x10^9$/L. The drug chart stated '1 pool of platelets' and did not specify the volume to be transfused. The nursing staff telephoned a junior doctor to request clarification of the platelet dose. The doctor stated that the verbal instruction was '15mL per kg'. The nurses misheard the prescription as '50mL per kg' and administered 300mL of platelets over 30 minutes. The infant suffered a cardio-respiratory arrest and was transferred to PICU where she died 2 days later.

Case 2 – faulty blood sampling technique and a wrong decision to transfuse

An 80-year-old female patient with a fractured neck of femur and expressive dysphasia from a previous stroke had a post-operative haemoglobin level reported as 3.9g/dL. The pre-operation Hb was 9.5g/dL and there had been little intra-operative blood loss. Eight hours following surgery the patient was noted to be restless, hypotensive and tachycardic. A junior doctor diagnosed hypovolaemia and prescribed 6 units red cells, all of which were administered over a 16 hour period. The post-transfusion Hb was 18.2g/dL, the patient subsequently died from cardiac failure. It was later realised that the blood sample with a Hb of 3.9g/dL was diluted by an iv infusion.

These two cases of 'inappropriate or unnecessary transfusion' are in a subsection of IBCT that has been increasing over the years. Altogether, between this category and the 'transfusion did not meet special requirements' category, there were 125 cases in which junior doctors were responsible for poor decision making in requesting or prescribing blood components. As these reports are not explicitly requested by SHOT, it is likely that this is an underestimate of the scale of the problem.

Clinical misjudgements occurring in this report include:

- Incorrect, written, over-prescribing of platelets for a baby
- Verbal prescription for rate and volume of a component
- Non-assessment of patient with apparently dangerously low Hb
- Over-prescription of red cells without clinical review
- Transfusion of patients with Hb above transfusion trigger
- Non-recognition of the symptoms and signs of a transfusion reaction
- Lack of awareness of the need or indications for irradiated components
- Lack of awareness of the need or indications for CMV negative components
- Over-reliance on laboratory results, and non-challenge of erroneous results
- Failure to review results in context of previous results, or to relate to clinical condition of patient
- Transfusion of red cells to asymptomatic patients
- Lack of knowledge about contents, volumes and use of components
- Inadequate handover to doctors working on subsequent shift

Two of the cases of lack of critical thinking and awareness resulted in fatality; the others, fortunately, did not – though many had the potential to do so. In some cases nursing staff and laboratory BMS staff attempted to prevent the inappropriate components being transfused, and were overridden. However, the responsibility for decision making and appropriate prescription of this potentially dangerous therapy is entirely medical, and it is the duty of doctors at all levels to understand the nature of the therapies they prescribe and their proper use and possible complications, and also to have awareness of their own limitations if they are not competent in these areas.

Transfusion medicine is an integral part of most hospital specialties, with a general working knowledge being a requirement for all hospital doctors if they are to be able to prescribe blood components effectively and safely. Many specialties have very specific complexities relating to transfusion, which doctors must at least appreciate to be able to ask for help when necessary – examples include haematology, obstetrics, transplant surgery, paediatrics and neonatology, healthcare of the elderly, and so on.

There are several possible contributory factors to the current situation, such as:

- transfusion is poorly represented in the curriculum and training of doctors; however, as a fundamental medical intervention integral to all specialties, it should be a core part of medical education
- lack of continuity of care of patients, so that, because of their rotas, doctors are unfamiliar with many patients they see
- short placements do not allow junior doctors to progress beyond initial familiarisation with a particular service before they have to move on
- loss of the apprenticeship culture in junior doctors training, with 'service' work taking place in the wards and 'training' happening on specific days away from the hospital, plus erosion of mentoring, and a reduced sense of the associated duties and responsibilities.

Transfusion medicine is unusual in that it has a nationwide collection system for specialty-specific adverse events data. Although this report relates to transfusion practice, is likely that this may be more broadly interpreted as being an example of a worrying trend in medical practice as a whole. Lack of communication or 'joined up' thinking can lead to sub-optimal patient care.

4. Recommendations

This year's key recommendations focus on the need for integration of transfusion medicine into the teaching and training curricula for junior hospital doctors, and nursing and scientific staff involved in transfusion. This goes beyond assessment of basic competencies and is recognising the need for solid knowledge and understanding of transfusion therapies so that sound decisions can be made in clinical practice.

As previously, these recommendations have been made after consultation with stakeholders to ensure support for their implementation. The final responsibility for ensuring action in relation to hospital-based recommendations lies with Trust Chief Executive Officers (CEOs), though the day to day responsibility may be delegated to members of the Hospital Transfusion Team (HTT).

All previous SHOT recommendations remain active, and are listed on the accompanying table together with updates on the implementation of relevant initiatives. In addition there are specific detailed recommendations at the end of each chapter aimed at improving patient safety in each specific reporting category.

The recommendations therefore appear in three sections this year:

- SHOT Recommendations of the Year
- Active recommendations from previous years: update
- Specific recommendations relevant to each reporting category (see chapters 5–12)

SHOT Recommendations of the Year

1. **Inclusion of transfusion medicine in core curriculum for junior doctors**: In this SHOT report there are two fatalities arising from incorrect decision making when prescribing components. In addition there are numerous cases of inappropriate transfusion and incorrect specifications of blood components given. As recommended in the 2002 report, it is imperative that the curricula of junior doctors in training in all hospital-based specialities include transfusion medicine. This must go beyond safe practice in patient ID and blood administration, and include core knowledge, clinical assessment and decision making when considering transfusion therapy. This cannot be delivered by competency testing alone, but requires that transfusion medicine is integrated into training in relevant specialities. A sufficient number of subspecialty trained transfusion consultants must be maintained to lead on education and training.

   Action: NBTC, JRCPTB (Joint Royal Colleges of Physicians Training Board), Royal Colleges of Physicians, Paediatrics, Pathologists, Anaesthetists, Surgeons, Obstetricians and Gynaecologists, the Academy Postgraduate Education Committee.

2. **Specialty accredited laboratory and clinical staff in all hospitals**: In the 2001 report SHOT recommended an ongoing programme of education and training of all staff involved in transfusion and this is reiterated this year. The NPSA safer practice notice 14[1] requires documented training of all relevant personnel, and competency assessments based around blood sampling, collection and administration practice. This is underway in many hospitals. However, all transfusion practitioners and a quorum of hospital transfusion laboratory staff must be trained to a higher level, and should be encouraged to achieve BBTS certification for laboratory practice or as transfusion practitioners. Hospital transfusion laboratories should ensure that an accredited transfusion specialist is available at all times.

   Action: Hospital CEOs, National Transfusion Laboratory Collaborative, BBT network, RCN, BBTS.

3. **Comprehensive reporting to SHOT by all hospitals**: Whilst the number of SHOT reports have increased year-on-year, this year has seen a slight downturn in numbers of reports. This is likely to be the effect of the implementation of the new system for reporting adverse incidents under the Blood Safety and Quality Regulations[3]. However, SHOT reporting, although 'voluntary' in statutory terms, is not voluntary in professional terms, and is a requirement for Clinical Pathology Accreditation (CPA) and the NHS clinical governance framework. Reporting to MHRA does not include the breadth of incident categories or detail of data reportable to SHOT and does not provide analysis and feedback to hospitals on adverse events. The joint SABRE web-based reporting system facilitates reporting to both MHRA and SHOT to fulfil both legislative and professional requirements.

   Action: Hospital CEOs, SHOT, Consultants with responsibility for transfusion together with HTC and HTT.

Active recommendations from previous reports: update

Year first made	Recommendation	Target	Progress
2005	Right patient – Right Blood – NPSA safer practice notice (SPN 14) as a result of a joint initiative with SHOT and NBTC.	Trust CEOs	Reduction in reports of ABO incompatible transfusions. Rolling out the introduction of competency assessments for clinical staff.
2005	Appropriate use of blood components.	Consultant haematologists with responsibility for transfusion, HTTs, HTCs	Overall reduction in red cell usage >15% in last 5 years nationwide. NCA platelet audit showed widespread inappropriate use of platelets and non-adherence to guidelines.
2005	Better laboratory practice – improved staffing levels, appropriate skill mix, competency assessment, safe on-call structures.	Hospital CEOs	National Transfusion Laboratory Collaborative set up to address this area – launched March 2007.
2005	Increase safety of routine anti-D prophylaxis.	Royal Colleges of Midwives, O&G, GP and HTTs	SHOT in obstetrics document in press. Several educational symposia aimed at midwives and O&G junior doctors have taken place. Highlighted as an area for action in BBT3.
2004	The RTC structure provides a potential forum for debate and sharing of problems and solutions in a supportive environment with expert clinical input. SHOT reportable incidents should be a standing agenda item for regional BMS forums and SPOT meetings. The RTCs should support translation of guidelines into local practice.	RTCs and user groups	NBS Hospital Liaison teams focused support on RTCs in 2005. RTCs setting up working groups in 2006. Realignment at RTCs with SHA regions in 2007.
2004	Further national initiatives are needed to drive forward blood safety issues in hospital transfusion laboratories.	NBTCs, with relevant professional bodies	Identified as a key recommendation in 2005. Launch of National Transfusion Laboratory Collaborative in 2007 aimed at improving laboratory practice.
2003	Hospital transfusion laboratory staffing must be sufficient for safe transfusion practice.	Trust CEOs	See above.
2003	BCSH guidelines on transfusion of neonates and children should be implemented.	RCPCH, RCN, staff in paediatric units and transfusion laboratories	SHOT 'Lessons for paediatric staff' produced 2006. 'SHOT in obstetrics' in press 2007. NBS Paediatric conference Feb 2007
2003	The NBTCs and counterparts should take a pro-active lead in driving forward blood safety issues in hospitals.	NBTCs	NBS Regional Hospital Transfusion Teams active in each region. Parallel initiatives in Scotland, Wales and Northern Ireland. Educational tools developed.

2002	HTTs must be established and supported.	Trust CEOs	Survey in 2004 (M Murphy and C Howell) showed 70% of Trusts had HTT but only 30% were supported. Survey in 2006 by MM/CH only said that 97% trusts had an HTC and 96% a TP.
2002	Blood transfusion must be in the curriculum for student nurses, medical undergraduates and newly qualified doctors.	GMC, PMETB, Undergraduate Deans, NMC	An education subgroup of the NBTC has been established. This group is linking with Deans of Medical Schools and Universities to get transfusion included in their curricula. SNBTS training package www.learnbloodtransfusion.org.uk endorsed in Scotland, Wales and NI.
2002	Blood transfusion should be in the curriculum of specialist trainees, especially anaesthetists and critical care nurses.	Medical Royal Colleges, Universities	Royal Colleges and Specialist Societies subgroup of NBTC established 2007.
2002	Blood transfusion should only be prescribed by authorised clinicians.		Endorsed by CMO Annual Report 2003.
2002	Mechanisms must be put in place for appropriate and timely communication of information regarding special requirements.	NBTCs, Trust CEOs	Card now available for patients requiring irradiated components. Further work needed. Carried forward as key recommendation for 2005.
2002	Resources must be made available in Trusts to ensure that appropriate and effective remedial action is taken following transfusion errors.	HAs, PCTs, Trust CEOs through HTCs and risk management structures	No mechanisms for monitoring.
2002	SHOT recommendations must be on the clinical governance agenda.	Trust CEOs, Trust Risk Management Committees and HTCs	No mechanisms for monitoring.
2001	An open learning and improvement culture must continue to be developed in which SHOT reporting is a key element.	Trust CEOs	Philosophy supported by NPSA. SHOT has developed a training tool for root cause analysis.
2001	An ongoing programme of education and training for all staff involved in transfusion.	NBTCs and network, Trust CEOs, NPSA/NBTC/SHOT initiative	Mandated by NPSA SPN 'Right Patient, Right Blood'. Also a requirement of NHSLA standards. Educational tool available at www.learnbloodtransfusion.org.uk, developed by SNBTS.
2001	Appropriate use of blood components must be strenuously promoted and evaluated. This must include monitoring for serious adverse effects of alternatives to transfusion.	NBTC, Trusts CEOs	Successive BBT initiatives promote this. NBS Appropriate Use Group and Patients Clinical Team active. Red cell usage has fallen by >15% since 2000. The National Comparative Audit programme has audited platelet use and use of blood in primary elective unilateral THR in 2006, upper GI bleeding in 2007.

2001	Transfusion practitioners should be appointed in all trusts.	Trust CEOs	Requirement of BBT2. Now appointed in 75% of hospitals (National Comparative Audit organisational audit 2005).
2001	More transfusion medical consultant time is needed in hospital trusts.		Requirement of BBT2, but national shortage of consultant haematologists.
2001	Existing procedures should be re-examined for flaws that could lead to systems errors.		BCSH guidelines on Blood Administration currently under review.
2000	Basic epidemiological research is needed into the timing and location of transfusions in the hospital setting.		'Where and when' study presented 2005 published 2007[6].
1999	All institutions where blood is transfused must actively participate in SHOT.	Trust CEOs	Requirement of BBT and NHSLA. Murphy and Howell survey indicated that 99% of responding hospitals (95% of NHS Trusts) participate. 69% reported events or Near Misses in 2005.
1999	Education in blood transfusion must be included in the curriculum for all clinical staff involved in prescribing and administering blood. All staff involved in the transfusion chain in hospitals must receive appropriate training, which must be documented. Effectiveness of training should be assessed by competency assessment.		See above.
1998	IT as an aid to transfusion safety should be assessed and developed at national level.	NBTC IT WG, NPSA/NBTC/ SHOT initiative, CfH	Co-ordination now achieved between NBTC, NPSA, CfH. National standard specification under development. Implementation is dependent on central funding through CfH or by individual Trusts.
1997	There is a need for a national body with relevant expertise and resource to advise government on priorities for improvements in transfusion safety.	DH	MSBTO reviewed by DH. New committee ACSBTO now in process of appointments.

5. Incorrect Blood Component Transfused

Definition

All reported episodes where a patient was transfused with a blood component or plasma product that did not meet the appropriate requirements or that was intended for another patient.

Four hundred and eighteen completed IBCT questionnaires were received. An additional case was transferred from the HTR section. Nineteen reports were withdrawn by the analysts, of which 13 did not meet the criteria for IBCT, and 6 were 'right blood to right patient' incidents, in which the patient received the intended component despite a serious breach of protocol. These are discussed separately at the end of this section. There were no reports of adverse events relating to autologous transfusion.

This section describes the findings from 400 analysed cases, a 17.5% decrease from 2005.

A striking feature this year is that for the first time there has been a reduction in the total number of reported cases of IBCT, even allowing for the decline in blood use over the past 4 years (see table 6). The reason for this reduction is not clear, and there are concerns that reporting may have been inhibited by early difficulties with the SABRE electronic reporting system, and by anxieties around the implementation of the Blood Safety and Quality Regulations.

It should be emphasised that the contents of SHOT questionnaires remain confidential to SHOT alone and also that adverse events in clinical areas not resulting in a reaction are not within the scope of the BSQR, and are therefore reportable only to SHOT.

It is essential that all events continue to be reported to SHOT if a comprehensive and ongoing understanding of transfusion risks in the UK is to be maintained.

Table 6
Rate of reporting 2003–2006 (excluding 77 anti-D Ig) per 100,000 components issued

Year	Number of IBCT reports	Reports per 100,000 components
2003	324	9.5
2004	372	11.1
2005	398	12.8
2006	323	10.6

The ratio of ABO incompatible transfusions to total IBCTs is unchanged from last year. Nevertheless, the continued reduction in numbers of ABO incompatible red cell transfusions (figure 4) observed this year, together with the marked reduction in the highest risk errors, where a patient received a blood component intended for a different patient or of the incorrect group, is encouraging. Providing reporting is complete, this may provide evidence that practice is improving, particularly in clinical areas.

The work of transfusion practitioners in improving standards is acknowledged and must be supported in Trusts.

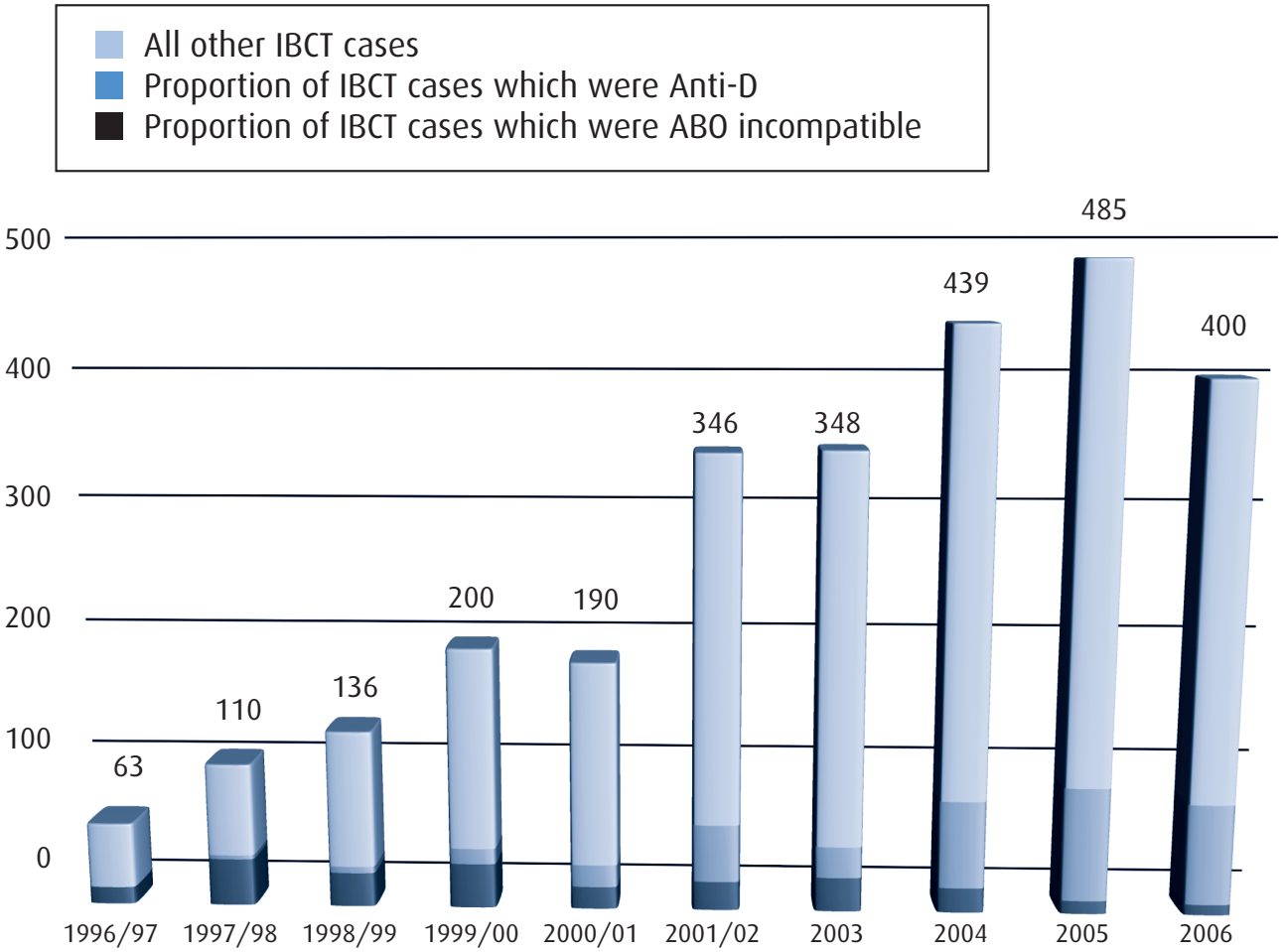
There is no cause for complacency, as 'wrong blood' events continue to occur where there has been failure to positively identify patients, either prior to blood sampling or prior to administration of blood. The practice of 'checking' blood away from the bedside, without a final patient identification check, often against a compatibility form, has not yet been eliminated. Implementation of the NPSA Safer Practice Notice 14[1] and NHS QIS Standards for Blood Transfusion[7] should remove this source of error.

SPN 14 has 3 action points:

- implement an action plan for competency-based training and assessment for blood transfusion staff;
- eliminate the use of compatibility forms as part of the final bedside check;
- examine the feasibility of using bar codes or other electronic identification systems, photo identification and a labelling system to match samples and blood.

It is of note that the 2 fatal IBCT cases this year were not caused by errors in blood administration, but were due to incorrect prescribing, in both cases involving junior doctors. Case 1 highlights the importance of careful prescribing in paediatric transfusion, and case 2 emphasises the need to match abnormal laboratory results to careful assessment of the clinical picture. Both cases reinforce the recommendation that blood should only be prescribed by a doctor who has undergone training in blood transfusion and has been assessed as competent [8,9].

Figure 4
ABO incompatible red cell transfusions



Patients

253 Females
146 Males
1 Not stated

Ages ranged from <1day to 99 years

Forty-seven reports (12%) related to patients under 18 years of whom 31 (8% of total IBCT reports, or 66% of cases in patients under 18) were infants under 12 months.

Mortality and morbidity

There were no deaths related to ABO incompatible transfusion, but 2 patients suffered serious morbidity following ABO incompatible red cells (cases 3 and 9 below, both imputability 3).

An infant aged 12 months died after rapid transfusion of an excessively large volume of platelets (Case 1 imputability 2).

An 80-year-old female patient died of cardiac failure following an unnecessary transfusion based on an incorrect haemoglobin level (Case 2 imputability 1).

Case 1 – lack of care and accuracy in paediatric prescribing results in overtransfusion

A very sick preterm infant, aged 12 months, with multiple congenital abnormalities, had been in hospital since birth and was scheduled for elective surgery. The platelet count was 48x10^9/L. The drug chart stated '1 pool of platelets' and did not specify the volume to be transfused. The nursing staff telephoned a junior doctor to request clarification of the platelet dose. The doctor stated that the verbal instruction was '15mL per kg'. The nurses misheard the prescription as '50mL per kg' and administered 300mL of platelets over 30 minutes. The infant suffered a cardio-respiratory arrest and was transferred to PICU where she died 2 days later.

Case 2 – faulty blood sampling technique and a wrong decision to transfuse

An 80-year-old female patient with a fractured neck of femur and expressive dysphasia from a previous stroke had a post-operative haemoglobin level reported as 3.9g/dL. The pre-operation Hb was 9.5g/dL and there had been little intra-operative blood loss. Eight hours following surgery the patient was noted to be restless, hypotensive and tachycardic. A junior doctor diagnosed hypovolaemia and prescribed 6 units red cells, all of which were administered over a 16 hour period. The post-transfusion Hb was 18.2g/dL, the patient subsequently died from cardiac failure. It was later realised that the blood sample with a Hb of 3.9g/dL was diluted by an iv infusion.

Learning points

- Prescriptions must be written by a doctor, and volume and rate of infusion must be clearly stated.
- Nursing staff must not accept verbal prescriptions or instructions, and should demand that prescribing protocols are followed.
- Medical and nursing staff should not work beyond their competence or expertise.
- All results, especially if highly abnormal, must be reviewed in the context of the patients recent history and current clinical condition.
- Large volumes of blood components must not be given without ongoing clinical and laboratory review.

Analysis of cases

IBCT case reports have again been analysed by category as follows:

Table 7

Type of event	Number (%)
'Wrong blood' events where a patient received a blood component intended for a different patient or of an incorrect group	54 (14%)
Other pre-transfusion testing errors (excluding erroneous Hb)	28 (7%)
Blood of the incorrect group given to recipients of ABO or D mismatched PBSC, bone marrow or solid organ transplant	8 (2%)
Transfusion of blood of inappropriate specification or that did not meet the patient's special requirements	108 (27%)
Inappropriate or unnecessary transfusions	51 (13%)
'Unsafe' transfusion where there were handling or storage errors	74 (19%)
Events relating to administration of anti-D immunoglobulin	77 (19%)
Total	**400**

In each subgroup, an attempt has been made to assess the contribution of errors in clinical areas and in laboratories.

1. 'Wrong blood' events (n=54)

These patients received a blood component intended for a different patient or of an incorrect group, and were put at risk of life-threatening haemolytic transfusion reactions.

- Eight patients received ABO incompatible red cell transfusions, 1 of whom was also D incompatible. Two suffered serious morbidity (both imputability 3) but survived.
- Three patients received ABO incompatible FFP (group O components given in error to patients of other groups). None suffered any adverse reaction, though 1 patient developed a positive DAT and agglutination on the blood film.
- Fifteen D negative patients inadvertently received D positive components (13 red cells, 2 platelets); 2 were female neonates, 1 a 4-year-old girl and 1 a 46-year-old female with a ruptured ectopic pregnancy. Eleven were males or elderly females. Three elderly females were subsequently found to have developed anti-D.
- The remaining 28 patients received components that were fortuitously compatible.

Causes of 'wrong blood' events

Table 8 shows the site of the primary error and also illustrates those cases where the primary error could have been detected at a later stage in the chain, but was not.

In 25/54 (46%) of cases the primary error was in the laboratory (*c.f. 42.5% last year*).

In 28/54 (52%) of cases the primary error was in a clinical area (*c.f. 57.3% last year*).

In 1/54 (1.9%) of cases the primary error was in the blood establishment (*c.f. 0 last year*).

Table 8
Site of the primary error that led to mis-transfusion

Site of Primary Error	No. of cases (%)
Sample from wrong patient	3 (6%)
Not detected by lab (previous group not noted)	*1*
Blood establishment	1 (2%)
Hospital laboratory failed to notice error	*1*
Not detected at bedside check	*1*
Laboratory error	25 (46%)
Not detected at bedside check	*7*
Wrong blood delivered to clinical area	15 (28%)
Not detected at bedside check	*15*
Blood administered to wrong patient	10 (19%)
Total cases	**54**
Total errors	**79**
Total errors in clinical areas	51 (65%)
Total hospital laboratory errors	27 (34%)
Total Blood Establishment errors	1 (1%)

Sample errors

Three cases were reported, 2/3 patients received ABO incompatible transfusions, of whom one suffered major morbidity.

Case 3 – Missed opportunities to avert a catastrophe

A 69-year-old female patient had a blood sample taken for a full blood count; the Hb was 8.9g/dL. As she was breathless a decision was made to transfuse her, and later the same day a 'doctors' assistant' was asked to take a further sample for repeat full blood count and a 2 unit crossmatch. The transfusion laboratory had no previous record of the patient. The Hb on this second sample was 9.9g/dL and the on-call BMS queried the need for transfusion, but was told that the patient was symptomatic and required the blood. The blood group of the sample was A D positive and 2 units were crossmatched and issued. Within 10 minutes of starting the first unit, the patient had a cardiac arrest. She was successfully resuscitated, the transfusion was halted and she was transferred to ITU. A further sample was sent to the laboratory for investigation of a possible transfusion reaction, but the on-call BMS was not alerted and did not carry out the investigation. The whole of the second unit was transfused in ITU early the following morning, surprisingly with no further apparent untoward effects. It appears that there was some discussion with the BMS prior to giving the second unit, but the possibility of an ABO incompatible transfusion was not considered.

Later that day the repeat sample was tested and grouped as O D positive. It was then realised that the sample taken by the 'doctors' assistant' for pre-transfusion testing was from another patient, who was not wearing a wristband and did not respond when asked to confirm her identity.

Learning points from this case

- Positive patient identification is an absolute prerequisite of blood sampling.
- Blood transfusion should only be undertaken at night if clinically essential.
- Unexpected discrepancies in laboratory results, such as occurred in this case, should be investigated and possible error considered.
- Clinical staff must be able to recognise a transfusion reaction and know how to proceed.
- A catastrophic transfusion reaction must be investigated urgently, with involvement of a consultant haematologist.
- The most senior doctor available should be involved in the decision to transfuse.

Laboratory errors

In 25 out of 54 (46%) 'wrong blood' reports the primary source of error was the laboratory. In another 2 cases previous mistakes, made in sampling and at the local blood establishment respectively, were not picked up by the laboratory when they should have been.

Fifteen of the errors occurred 'out of hours', 8 within normal working hours and 2 reports did not state the time of the error. Staff involved in the errors included 14 BMS staff who were transfusion specialists and 8 who did not work routinely in transfusion but were covering transfusion 'out of hours'. Two cases involved locum staff and in one report no information about the staff was given.

In 2 cases the wrong sample was selected for testing resulting in a wrong ABO group determination. Fortuitously neither error resulted in an ABO incompatible transfusion.

Case 4 – a basic error that might have been disastrous

When grouping the patient's sample, the duty BMS picked up the sample from another patient, consequently the group was incorrectly determined as A D neg instead of O D pos. Luckily, as the laboratory was short of A D neg red cells, O D neg was crossmatched and was compatible.

Eleven reports of grouping errors were received, 4 ABO and 7 D typing errors. 7 reports involved manual ABO/D techniques. In 6 of these cases the method used was the laboratory's manual, 'urgent' method and in one case the laboratory's manual, routine microplate method. In most cases the source of the error could not be clearly identified – reporters have queried either misreads or transcription errors. Only one report could prove a transcription error as the correct D type was written on a worksheet but then incorrectly entered onto the blood bank computer system.

In 3 cases automated systems were used for blood grouping but incorrect manual interventions resulted in the wrong D types being reported. In 2 of these cases false positive weak reactions were obtained with the anti-D reagent in use on the analyser and laboratory protocols to repeat the D type with a second anti-D were not followed. In a third case an incorrect blood group was manually entered into the blood bank computer following an edit of a weak reaction. All 3 patients produced anti-D. In the final case a group $A_{weak}B$ with anti-A1 was mistyped as a group B on an automated system. This was discovered some time later when a repeat sample came into the laboratory. The anti-A_1 had disappeared, causing a grouping discrepancy between the forward and reverse group; a manual tube group was performed and a reaction with anti-A obtained.

Seven reports involved component selection errors. These were divided between those in which there did not appear to be any computer warnings that may have helped prevent the error and those in which computer warnings were overridden or not properly read. For example:

Case 5 – computer warning overridden

Two units of red cells were requested for a 79-year-old female patient on ITU. The patient's blood group was AB D neg but the BMS selected group A D pos blood and issued 2 units. The 2 units were transfused and the error was discovered when a sample taken for a group, and saved the following day grouped as A D neg. The laboratory system had flagged that the group was incorrect when the A pos blood was reserved but the BMS did not heed the warning. As the patient was AB D Neg the computer system flagged to say that blood of another ABO group was being issued. The BMS saw this warning but did not take into account the D group.

Labelling errors occurred in 5 cases. In 3 cases labels for 2 patients where blood components were being issued simultaneously, were transposed. In one case a unit of red cells that had not been crossmatched for that particular patient was labelled and in the final case, during an emergency situation, FFP left the laboratory without any labels attached to the packs. A report form with the numbers of the packs was issued.

Case 6 – failure to label correctly

The BMS crossmatching blood put a compatibility label on a unit of blood that was not matched for this patient (it was the same blood group) and issued the blood without completing the required checks. The ward staff then transfused this unit to the patient without completing the required checks.

In a number of the above cases it appears that basic, manual checks are being omitted or performed inaccurately, often during emergency situations.

This year has shown a reduction in the number of laboratory errors leading to 'wrong blood' events, although laboratory errors, as a percentage of errors made, has increased.

The following table shows the marked decrease in ABO typing errors this year:

Table 9

Year	Total No of Cases	Wrong Sample Tested	Interpretation /Transcription Errors	Other	ABO Incompatible Transfusions	Sequelae
2003	17	8	9		7	2 major morbidity
2004	18	5	12	1	6	1 death 1major morbidity
2005	22	9	12	1	9	1 AHTR
2006	6	2	3	1	0	No morbidity

Five of the 6 cases of ABO errors this year involved mistakes in manual testing, or mistakes in a manual step during automated testing, as did all the errors in D typing. In previous years the majority of ABO and D typing errors also occurred during manual testing.

The reduction in ABO typing errors seen this year is encouraging and there is some anecdotal evidence that laboratories have taken on board the messages of previous SHOT reports and have moved further away from manual testing. For example, automation is being used more often in emergency situations and greater numbers of out-of-hours staff have been trained in the use of available automation. However, there is also some concern that reporting may be incomplete as the decrease in errors has coincided with the commencement of MHRA inspections and, again anecdotally, there is a perception amongst reporters that an ABO typing error may initiate an MHRA inspection.

Learning points

- Training and competency assessment in the laboratory must cover basic manual checking procedures to ensure that these are second nature at a time when automation and computerisation will have lessened experience and practice in these basic skills.

The following learning points from last year's report remain pertinent:

- Competency-based training for laboratory staff must include those working out of hours.
- A laboratory quality system, as required by the Blood Safety and Quality Regulations, must include internal incident reporting mechanisms and appropriate, documented, corrective actions.

Root cause analysis should be performed where there are adequate resources when a 'wrong blood' incident occurs, as these incidents potentially have the most serious outcomes. For example, in the 3 cases above, where a manual intervention was required on an automated system, questions must be asked about the reagents that gave the weak, false positive results as well as the process of manual intervention that failed.

Collection and administration errors

In 15 cases, the wrong blood was collected from the issue location and an inadequate pre-transfusion check failed to prevent its administration to the patient. Three resulted in ABO incompatible red cell transfusion.

In 7 of these cases, blood for a different patient was taken to the clinical area and in 6/7 cases was 'checked' against a compatibility form, with no final bedside identification check.

Five cases involved incorrect use of 'emergency O negative' blood.

In 3 cases, blood was delivered directly from a blood centre to a clinical area and transfused, bypassing the transfusion laboratory and in a further case highlighted earlier, unlabelled FFP was taken from the blood bank and transfused.

In a further 10 cases, the correct component was delivered to the clinical area but was given to the wrong patient.

In 7 of these cases the blood was checked away from the bedside against a compatibility form, and then taken to the wrong patient.

Of particular concern were 2 cases in which, when the error was discovered, the unit was taken down, the giving set changed and the remainder of the unit transfused to the intended patient. These cases, together with 2 reported in the 'unsafe' section in which the blood pack was accidentally punctured then resealed and the transfusion continued, illustrate a worrying lack of understanding of the potential risks of bacterial contamination of blood components.

In 1 case the wrong twin neonate was transfused. Two cases related to 2 patients in adjacent beds on a gastro-intestinal unit, both with obstructive jaundice and requiring invasive procedures, for whom FFP was prescribed. Eight units of FFP, 4 for each patient, were placed on a table between the 2 beds but were transposed. One patient received ABO incompatible FFP.

Case 7 – same name pitfall, colleagues trying to be helpful, and compatibility form used to check

A porter arrived in blood bank to collect 6 units of blood urgently required in ITU for a 76-year-old male patient, but did not take the required documentation with the patient details. He collected blood for another patient with the same surname.

The blood was received by the ITU Sister who informed the patient's named staff nurse that it had arrived, and placed it by the patient's bed, as the named staff nurse was occupied. Another nurse offered to put it up, and asked a student nurse to assist with the pre-transfusion check. Together they checked the unit of blood against the compatibility form and started the transfusion. The nurse then checked the ID number on the prescription sheet against the unit bag, realised it was the wrong blood and immediately stopped the transfusion. The blood was group A, the patient group O.

Case 8 – failure of checking procedures in a night-time transfusion

An 84-year-old female patient (alias Ellen Johnson) was admitted to a medical ward for elective blood transfusion. As the ward was full, she was moved to a surgical ward, which received a total of 10 'boarding' patients that day. Another patient with a similar forename and surname (alias Ella Johnston), with crossmatched blood still assigned to her in the surgical satellite refrigerator, had been discharged from the surgical ward that morning.

Sometime between midnight and 0800 hours, the surgical ward nursing staff telephoned the porters to request collection of the blood for Ellen Johnson, but gave the forename and surname only. The porter went to the surgical satellite refrigerator, without taking the standard documentation for blood collection, and collected a unit of blood labelled for Ella Johnston. The blood for Ellen Johnson was in a different location, as it had been requested from the medical ward. The blood was 'checked' by 2 nurses against the patient's notes and wrist band, but the discrepancy was not noticed until the second incorrect unit was delivered to the ward by porter. Fortunately both patients were group O D negative, with no clinically significant alloantibodies.

Case 9 – multiple errors in an emergency transfusion

A 51-year-old male was admitted to A&E with a haemopneumothorax. A chest drain was inserted, the drainage was heavily bloodstained, and a venous sample was sent to the laboratory requesting 4 units of blood urgently. The patient's blood group was O D positive and 4 units of crossmatched blood were placed in the issue refrigerator, located in a small room off the main hospital corridor. The A&E department was notified that the blood was ready, and a porter was sent to collect it. There was a power cut in the hospital and the porter could not see to sign out the blood, so summoned a colleague to bring a torch. Using faint light, the 2 porters removed all 4 units of blood, but did not check the patient details against the issue sheet.

In the A&E department, 2 nurses 'checked' the patient details and component ID numbers against the compatibility form, but did not check the patient's wristband or ask him to identify himself. No observations were carried out during transfusion of the first unit of blood. When the second unit was commenced the patient complained of feeling unwell and was found to be hypotensive. At this point it was realised that the wrong blood had been collected and administered, and this group O patient had received 1.5 units of group B blood intended for another patient. The patient was admitted to ITU for management of an acute haemolytic reaction and made a complete recovery.

Other errors noted in the process were; that the blood was not prescribed until the first unit was in progress and the wrong surname was written on the transfusion chart. All 4 crossmatched units were removed from the blood bank and, even had the transfusion gone according to plan, 2 would have been out of temperature control.

Case 10 – night time transfusion, lack of wrist band, understaffing and lack of training made this a high-risk situation

Two elderly females were admitted to an orthopaedic ward at night, both with a fractured neck of femur. The ward was understaffed because of sickness and the nurses on duty had not recently received transfusion training. Patient A required transfusion, the urgency of which is not clear. Blood was crossmatched, issued and delivered to the ward, but was given to patient B, a 95-year-old female with dementia who was not wearing a wristband (the nursing staff were waiting until a printed ID band was sent to the ward from the central bed bureau and were unable to confirm her identity). The blood was compatible.

Learning points from these cases

- In all of these examples, staff were working under pressure and against difficulties, e.g. understaffing, power cut, excess workload, and were giving of their best efforts under adverse circumstances, but not realising that 'helping out' by doing someone else's job may increase risk.
- Staff should be educated to adhere to established safe procedures at all times, except in cases of extreme clinical urgency, which may justify the increased risk of deviation.
- High risk situations (such as simultaneous transfusion of patients in adjacent beds) should be recognised and, if unavoidable, special care taken with identification.
- Compatibility forms and patient notes MUST NOT be used as part of the final check at the patient's side[1].
- As recommended last year, blood administration outside of core hours should be avoided unless clinically essential.

2. Laboratory pre-transfusion testing errors (n=28)

Cases where antigen negative blood should have been selected for a patient with a previously known antibody but was not, are included in the 'Special requirements not met' section.

Of the 28 cases reported, 14 occurred 'out of hours', 13 in normal working hours and in 1 report the time was not stated. Twenty-one of the errors involved BMS staff who regularly work in transfusion and 7 involved BMS staff covering transfusion 'out of hours'.

The errors can be divided into testing/interpretation errors, i.e. where a test was not performed/interpreted correctly (6 errors) and procedural errors i.e. SOPs were not followed (22 errors). In one case two procedural errors occurred.

Testing errors included missing weak antibodies (4 cases). Three of these were antibody screens that gave negative results when performed manually but were then found weakly positive when repeated by automated methods. Two reporters cited extending automation to 'out of hours' as a corrective action that presented a training issue. Other problems occurred in antibody interpretation and phenotyping.

There were miscellaneous procedural errors. In 5 reports electronic issue had been used inappropriately when antibodies were present on the historic file or when an antibody identification was still outstanding. Other errors included using samples that were too old (7 cases), failing to consult maternal results when supplying blood to neonates and failing to link historic and current records, thus missing important antibody information.

In a number of cases robust lines of communication did not appear to be in place within the laboratory so that information available to one BMS was not picked up by the next BMS dealing with the case.

Case 11 – failure to check the age of sample

Two units of red cells were electronically issued on a specimen number that was over a-year-old. No formal compatibility testing was performed. The patient suffered a mild transfusion reaction (rise in temperature). A current sample was then located from the haematology laboratory and tested. The sample contained no atypical antibodies and the red cells were compatible retrospectively.

Case 12 – inappropriate use of electronic issue

Blood was accidentally issued electronically for a patient with a positive antibody screen. The error was detected the following morning during routine hours when the BMS on the antibody bench noticed that blood had already been issued on the sample that she was performing an antibody identification panel on. The antibody was identified as anti-E. By this time, the patient had been transfused 2 of 4 units, one of which was E positive. At the time the report was submitted to SHOT, the patient was being monitored by the consultant haematologist.

Case 13 – use of multiple patient identification numbers creates a hazard

A sample for group and save was entered into the computer with a Trust number. The BMS booking in the request failed to notice a previous record indicating the presence of anti-K. The antibody screen was negative. During the on-call period a crossmatch was added to the request and 6 units of blood were issued urgently, before the BMS on call realised that there was another record for the patient showing the anti-K. All 6 units were K negative. The two records were waiting to be merged.

Case 14 – failure to record an antibody specificity and use of a sample that was too old may have contributed to a death

Blood was originally transfused on the 9th and 10th of the month when the patient underwent CABG with subsequent complications. The patient had a known, single antibody at this stage (anti-Fy^{a}). A further blood sample was taken on the 13th and used to crossmatch blood for transfusion on the 16th. A new request for crossmatch was received on the 21st as the patient was anaemic. This sample revealed a new antibody (anti-Jk^{b}) and it was shown that the patient was undergoing a delayed haemolytic transfusion reaction. On laboratory investigation into the case 2 errors were uncovered: the sample used for transfusion of blood on the 16th was too old; as the patient had been recently transfused the sample used should have been taken within 24 hours of the next transfusion. When the antibody identification panels from the 13th were checked it was found that an anti-Jk^{b} had been detected but had not been entered onto the transfusion computer. The patient subsequently died as a result of the post-CABG complications, although the DHTR may possibly have been a contributory factor.

Learning points

- Laboratories must ensure that robust systems are in place for highlighting 'outstanding' work on a patient, for example patient records awaiting merging, incomplete antibody identification.
- Laboratories should follow the comprehensive guidance on the electronic selection and issue of units given in the BCSH guideline: 'The specification and use of IT systems in Blood Transfusion Practice'. Some pertinent points from this document are:
  - Robust procedures and strict adherence to protocols is essential to ensure safe working practices.
  - All electronic issue procedures should be controlled by computer algorithms to validate appropriateness of actions.
  - For previously transfused patients, the timing of the sample must comply with BCSH guideline 'Compatibility Procedures in Blood Transfusion Laboratories'[10].
  - The patient's serum/plasma does not contain, and has not been known to contain, clinically significant red cell alloantibodies reactive at 37°C.

3. Blood of wrong group given to recipients of ABO or D mismatched haemopoetic stem cell and solid organ transplants (n=8)

- 5 ABO mismatched haemopoetic stem cell transplants
- 2 D mismatched haemopoetic stem cell transplants
- 1 ABO mismatched liver transplant

The liver transplant patient suffered severe haemolysis resulting in acute renal failure, but this was not considered to be caused by the transfusion (imputability 0). The remaining 7 patients had no adverse reactions to transfusion.

In 5 of these cases the requestor did not inform the laboratory that the patient had received a mismatched transplant. One of these should have been detected by the laboratory finding a discrepant reverse group.

In 3 cases the primary error was in the laboratory, including 2 where the BMS failed to take note of a computer 'flag'.

Three of the 4 cases in which there was a laboratory error were tested outside normal working hours by a BMS who did not normally work in transfusion. The degree of urgency is not clear.

Learning points

- Clinical staff must ensure that the transfusion laboratory is fully aware of these complex cases, and unless there is extreme urgency, pre-transfusion testing should be done by experienced staff during normal working hours.
- A mechanism for communication of transplant details between clinicians and laboratories must be in place.

4. Transfusion of components of inappropriate specification or that did not meet special requirements (n=108)

The number of these cases is reduced from last year, particularly those requiring irradiated or antigen negative blood. Irradiation is now carried out exclusively by Blood Establishments but it is unclear what effect this might have on adverse event reporting rates. Nevertheless, 82 patients were placed at risk of TA-GvHD. There were no adverse outcomes in this category.

Table 10
Special requirements not met

Special requirement	No. of cases
Irradiated components	77
CMV negative components	9
Irradiated and CMV negative	5
Antigen negative red cells for patient with known antibody	7
Phenotyped or K-neg red cells	2
Neonatal/paediatric red cell transfusion,	4
Viral inactivated single donor non-UK FFP for children <16	4
Total	**108**

Table 11
Sites of the errors that led to failure to provide special requirements

Site of Primary Error	No. of cases (%)
Request errors	79 (73%)
Also laboratory error	18
Also bedside error	24
Blood establishment errors	4 (4%)
Also hospital laboratory error	1
Hospital laboratory errors	23 (21%)
Also bedside error	10
Unsuitable component collected	2 (2%)
Also bedside error	2
Total cases	**108**
Total errors	***163***

In 38 cases there was failure to request special requirements and no means of detecting these requirements at a later stage (in the laboratory or at the bedside). In 19 of these cases patient care was shared between 2 healthcare organisations and the need for the special requirement was not communicated to the organisation where the patient was being transfused.

Learning point

- A formal mechanism needs to be introduced for informing other hospitals of patients' special requirements.

Table 12
Indications for irradiated products (n=82)

Indication for irradiated components	No. of cases
Purine analogue therapy	29
Stem cell transplantation	8
Hodgkin's Disease	19
Di George syndrome (confirmed or suspected)	5
SCID	2
Severe aplastic anaemia/ALG	1
Neonate, previous *in utero* transfusion	2
Miscellaneous *	16
Total cases	**82**

* Includes cases in which the indication for irradiation is unclear, or appears to be in excess of current BCSH guidelines

Case 15 – use of multiple patient identification numbers creates a hazard (again)

A 34-year-old female patient with Hodgkin's Disease was admitted to the local hospice for top-up transfusion. The request was made using a hospice admission number, not the Hospital number, and the previous transfusion laboratory history was therefore not found. The request form stated 'Hodgkin's Lymphoma' but the box requesting irradiated components had not been ticked. The BMS 1 doing the crossmatch did not recognise the need for irradiated blood.

Cases 16, 17, 18, 19, 20

These 5 infants aged between 10 days and 4 months and with a confirmed or suspected diagnosis of Di George Syndrome, received non-irradiated blood components during cardiac surgery. In 4 cases, the blood request did not specify irradiated components, though the diagnosis was written on the request form. In the fifth, the diagnosis was made during the operation and irradiated components were requested, but the previously ordered, non-irradiated blood was used.

CMV negative components (n=14)

The balance of evidence from clinical studies suggests that acceptable CMV safety can be achieved by pre-storage leucodepletion[11], however CMV seronegative cellular components continue to be requested and provided for CMV antibody-negative pregnant women, CMV antibody-negative recipients of allogeneic stem cell transplants, intrauterine and exchange transfusions and patients with HIV disease[12]. No case of transfusion-transmitted CMV has been reported to SHOT.

Antigen negative red cells for patient with known antibody (n=7)

All but 1 of these cases were laboratory errors, including 1 error by a reference laboratory

One case was reported where the patient was known to have anti-e, but emergency group O D negative blood was taken from a satellite refrigerator in an emergency. Anti-e had been found on the pre-op sample & reported. The patient was taken to theatre without checking the blood group and antibody results, thus not requesting appropriate blood in advance. When uncontrolled bleeding occurred emergency O negative (rr and thus e positive) was used without contacting and consulting with the laboratory. The laboratory did have type-specific blood available in stock that could have been issued as type specific immediately had they been asked to do so.

Phenotyped or K-neg (n=2)

One was a patient with sickle cell disease, and one a young female, where hospital policy was to provide K negative blood.

Neonatal transfusions (excluding irradiation) (n=4)

In 2 cases 'adult' group O D neg blood was taken from a satellite refrigerator for a neonate in extremis.

One case was of red cells in SAG-M provided for a neonatal exchange transfusion because the reason for transfusion was not stated in the verbal request.

One case was of 'adult' red cells provided by blood bank staff for a 9-month-old infant because the volume requested was greater than 1 paedipack.

Failure to issue viral-inactivated non-UK FFP for a child less than 16 years (n=4)

Four cases were reported. In two the FFP was required urgently and MB was not readily available.

In a further two cases a computer flag might have ensured selection of correct component.

Learning points

There are opportunities throughout the transfusion chain where special requirements can and should be documented and communicated. There should be formally established communication channels, supported as far as possible by information technology.

- Bone marrow transplant units must have a robust mechanism in place for communication of special transfusion requirements, and responsibilities must be clearly defined.
- Arrangements for shared care must specifically include communication of special transfusion requirements.
- Identifying the need for special transfusion requirements is ultimately a clinical responsibility and the requirement must be clearly indicated on the request form and the blood prescription. The design of such documents should facilitate this and prescriber education is required. The use of an e-form may improve accuracy and facilitate the process.
- There should be local protocols empowering blood transfusion laboratory staff to ensure that appropriate clinical information is provided with requests for blood transfusion. It is not the responsibility of the laboratory staff to recognise clinical conditions indicating special requirements, but they can provide an additional safeguard and should check the clinical and demographic details on the request form.
- IT 'flags' should be used wherever possible, e.g. date of birth warnings, transplant patient.
- The pre-transfusion check at the bedside must include checking of special requirements against the prescription.
- When purine analogues are prescribed for a patient this should be immediately communicated to the transfusion laboratory so that the patient record can be appropriately 'flagged'. This can be effectively achieved by automatic download from the pharmacy to the laboratory computer.
- A histological diagnosis of Hodgkin's Disease should trigger a communication to the transfusion laboratory. Again, this can be supported by a link between the histopathology and the transfusion laboratory computer systems.
- Cardiac surgical units undertaking correction of congenital heart defects must be aware of the requirements for irradiated blood for patients with confirmed or suspected Di George Syndrome.
- The need for irradiated components must be clearly indicated in the patient's case notes and on blood component prescription chart.
- The patient must be educated regarding the requirement for irradiated components and provided with written information and a card.

5. Inappropriate or unnecessary transfusions (n=51)

These cases are important as they carry a high risk of mortality and morbidity, this year accounting for 2 deaths (see cases 1 and 2 above).

In 37/51 of these cases the decision to transfuse was made on the basis of incorrect information.

- In 21 cases this was due to an FBC result from an unsuitable sample, e.g. taken from the same arm as an i.v. infusion, or allowed to settle in a syringe, or containing clots.
- In 1 reported case the sample for FBC was taken from the wrong patient.
- Four cases were due to wrong analytical results, 2 from the haematology laboratory and two near patient testing, one of which was a derived Hb result from a blood gas analyser.
- In 7 cases the full blood count result was misinterpreted or wrongly entered into the patient's notes.
- In 4 cases the cause of the error was not clear.

In all of these cases it could be argued that there was also a requesting/prescribing error, in that the decision to transfuse was made on the basis of a laboratory result, without sufficient attention to the clinical picture. This is discussed in more detail in the Key Message (p. 17).

Nine cases, including one fatality, involved a prescribing error, and in 5 the wrong component (e.g. platelets instead of FFP) was collected from the blood bank and transfused.

The errors leading to inappropriate or unnecessary transfusions are summarised in table 13.

Table 13
Sites/stages of errors leading to inappropriate transfusion

Primary error	Number
Unsuitable sample for FBC, e.g. from 'drip arm' or from wrong patient	22
Also laboratory failed to note unsuitable sample	*4*
Analytical error (haematology laboratory)	2
Analytical error (near-patient testing)	2
Reason for wrong result not known	4
FBC misinterpreted or wrongly transcribed	7
Prescription error (incorrect volume or rate, failure to check FBC)	9
Wrong component collected from blood bank	5
Total cases	**51**
Total errors	**55**

Case 21 – faulty sampling technique, poor clinical decision making and lack of formal handover result in unnecessary transfusion

An 88-year-old female patient was recovering from elective surgery. Blood samples for full blood count and biochemistry were taken by a junior doctor from the same arm as a saline infusion, resulting in a falsely low Hb (6g/dL). The junior doctor ordered and prescribed 4 units of red cells. The registrar on duty recognised that the results did not fit in with the clinical condition of the patient and asked for the investigations to be repeated. A further sample was sent to the laboratory, but was not requested as urgent and was labelled with a different hospital number. The sample was received in the laboratory following a shift change, and because of the different hospital number the BMS did not recognise the discrepancy in the results. The repeat Hb was 12g/dL, the result was not telephoned to the ward but was sent electronically. The junior doctors had also changed shifts, the doctor coming on duty was not aware of the repeat sample and the 4 units were transfused. The post-transfusion Hb was 18g/dL. No ill effects were reported.

Case 22 – incorrect telephone transcription triggers unnecessary hospital admission and transfusion

A 62-year-old female attended her GP complaining of headache; a full blood count and ESR sample were sent to the hospital for testing. The ESR was elevated and the clinical details prompted the laboratory to telephone the GP surgery with the results, which included Hb 12.4g/dL. The results were written on a scrap of paper by the receptionist and later transcribed into the doctor's log. The original paper was destroyed. The Hb was recorded in the log as 4.4g/dL. The GP saw the patient again the following day and arranged for her urgent admission for transfusion and investigation of anaemia. The admitting doctor noted that she had no symptoms of anaemia but nevertheless proceeded with transfusion. Further blood samples were taken but the transfusion was commenced before the results were available. The repeat Hb of 12.3g/dL was telephoned to the ward, the transfusion was stopped and the patient discharged.

Case 23 – consultant fails to keep up to date with transfusion practice

A consultant verbally instructed a junior doctor to prescribe '5 packs' of platelets (intending 1 ATD) for a 68-year-old male patient with leukaemia. The BMS queried the request, but was overruled as it had been a consultant instruction.

Learning points from these cases – some still pertinent from last year

- All staff undertaking phlebotomy must understand the importance of correct patient identification and correct sampling technique and must be assessed as competent.
- Blood should only be prescribed by a doctor who has undertaken training in blood transfusion and has been assessed as competent.
- Laboratory results must be evaluated in the context of careful clinical assessment of the patient.
- Implementation of shift systems requires an arrangement for formal handover.
- Formal protocols are needed for telephoning of laboratory results, including 'read-back'.
- There should be local protocols empowering blood transfusion laboratory staff to query clinicians about the appropriateness of requests for transfusion against local guidelines for blood use.
- Analytical errors involving point of care testing (e.g. erroneous Hb results obtained from blood gas analysers) should be reported to the MHRA Medical Devices division so that they can be investigated with the manufacturer of the device, and any problems disseminated to all users. Reports can be submitted electronically or forms downloaded from the MHRA website www.mhra.gov.uk.
- Consultant staff should ensure that they keep up to date with current transfusion practice.

6. 'Unsafe' transfusions (n=74)

These cases might be regarded as relatively low risk, but many give cause for concern, particularly the handling errors in clinical areas.

Table 14

Type of error	Number
Blood out of temperature control	33[a]
Blood component given was past its expiry or suitability date	25[b]
Blood components transfused over an excessive time period	11
Other handling errors	5[c]
Total	**74**

[a] There were 7 cases where blood was out of temperature control during transfer between hospitals (2 were community hospitals) or to off-site units.

In 13 cases blood was out of the refrigerator for >30 minutes, then returned to stock and later transfused.

In 8 cases blood was out of temperature control in a clinical area (e.g. in a ward drugs refrigerator).

There were 5 blood refrigerator failures.

[b] Thirteen patients received expired components (5 where component expired at midnight and was transfused before it could be cleared from stock the next morning). There were cases of recently transfused patients where the period of suitability of the blood had expired.

There was 1 case of FFP given after its post-thaw expiry.

[c] In 2 cases the blood pack was punctured by the giving set spike and sealed with tape.

In 1 case where a blood warmer was not available and a red cell unit was immersed in a bowl of warm water.

In 1 case FFP was thawed by a locum BMS in a bucket of water as the correct equipment was broken. In these circumstances a thermometer should have been used to monitor the temperature but this was not done.

In 1 case a large clot was found in a unit of red cells during transfusion.

There were 4 cases that occurred outside an acute hospital setting (2 in community hospitals, 1 GP unit, 1 in a hospice). These numbers are small, but highlight the importance of correct handling. Denominator data is not currently available for the number of transfusions taking place in the community, but it must be made clear that transfusion guidelines and policies apply to all settings in which blood is given.

7. 'Right blood to right patient' (RBRP) (n=55)

As in previous years, we have given reporters the opportunity to separately submit incidents where the right blood was transfused to the right patient despite one or more errors, which should have led to the unit being rejected. These incidents do not fit the definition for IBCT but are, nevertheless, instructive. They are not included in the overall numbers of IBCT cases. Six cases originally sent as IBCT by reporters were transferred to this section.

The 55 cases are summarised in table 15

Table 15
Right blood to right patient episodes

Elements that were wrong on blood packs, documentation, identity bands, etc	Number of incidents
Name alone or with other elements	17
DOB alone or with other elements	15
Transposed labels on 2 units	9
Hospital or NHS number	8
Incorrect unit signed for in transfusion lab records	2
Units unlabelled	1
Miscellaneous:	
Incorrect address used on sample and form	1
Old compatibility form used to check units in theatre	1
Laboratory data entry error for component blood group	1

Regardless of what the error was, where it was made or by whom, the vast majority of these transfusions (98%) should have been prevented by one or more checking procedures.

Table 16 shows where the error(s) should have been picked up but were not or were ignored.

Table 16
The checking procedure(s) that failed to detect the error(s)

Checking procedure	Number of incidents
Laboratory + bedside checking	20
Sampling + bedside checking	17
Sampling + laboratory + bedside checking	6
Collection + bedside checking	3
Patient registration + bedside checking	3
Sampling + laboratory	2
Blood centre + laboratory + bedside checking	1
Laboratory + collection + bedside checking	1
Bedside checking	1
Clinical decision to proceed	1

In IBCT cases, except in very unusual circumstances, if there was a clinical decision to transfuse despite the component being in some way unsuitable, the incident would not be included in the analysis. However, in the case of 'right blood to right patient', clinical decisions are often taken because the clinician is unable to see the potential for error and such decisions are made in routine situations as often as in emergencies.

RBRP case 3

A patient was admitted to ITU, from where a request for platelets was received with an incorrect DOB on the sample and form.

The BMS on duty altered the laboratory computer record to fit with the incorrect information and issued the platelets.

Several days later, another request was made, this time with the correct DOB, and the error in the laboratory was corrected.

RBRP case 6

Two units of blood were crossmatched for a patient, and one was transfused pre-operatively on a ward.

The second unit was required in theatre, but the compatibility form had not been sent to theatre with the patient's notes. A consultant anaesthetist carried out the checking procedure using a compatibility form from a previous transfusion, which was in the notes.

RBRP case 39

A patient was admitted using details from an old prescription sheet in the notes, which contained an incorrect hospital number. This number was then transcribed onto a new prescription sheet, nursing notes, care pathway and wristband.

Patient ID labels containing the correct details were printed from the electronic patient record, then used on the sample and request form for transfusion.

The discrepancy was discovered during the bedside check on the third unit of blood for this patient.

5.1 Errors related to IT systems

As noted in last year's report, problems with IT systems (or their incorrect use) continue to cause IBCT incidents. In 2006, there were 27 cases (28 errors) that led to the transfusion of an incorrect component (see Table 17).

Table 17

Error	No. of reports	Non-irradiated unit transfused	Antigen positive unit transfused	Non-CMV Neg unit transfused	Other	BMS works routinely in Lab
Records not merged	6	2	4	0	0	3/6
Computer system 'down'	6	3	1	1	1 (transcription error)	6/6
Historical record not consulted	3	2	1	0	0	2/3
Protocols for searching previous records insufficiently flexible	3	3	0	0	0	2/3
Ignored warning flag	2	1	1	0	0	1/2
Data not transferred from old system	1	0	0	0	1 (ABO mismatch)	1/1
Failure to update warning flags	1	0	0	0	1 (MB-FFP for a child)	0/1
Inappropriate electronic issue	6	0	4	0	2 Protocol violations	5/6

Patients often acquire multiple hospital numbers (4 in one instance) and case records. It is essential to merge records regularly so that warning flags are not missed by accessing the 'wrong' computer record. Implementation of the NHS number, as recommended by NPSA[13] , will reduce this risk.

'Down time' on the laboratory computer system, making the transfusion record inaccessible, was responsible for 6 incidents. In 1, mis-transcription of a phoned Hb result led to an inappropriate red cell transfusion. During scheduled down time, non-essential transfusions should be avoided and it is important to have robust back-up and recovery procedures.

In 3 cases the BMS did not consult the historical record and, in a further 3 cases, an inappropriate search strategy failed to locate previous records with a warning flag. In 2 cases the warning flag was ignored or overridden for unclear reasons. In more than half of these cases (5/8) the BMS worked regularly in the transfusion laboratory.

Warning flags indicating requirement for newly available components were not updated and, as a consequence, a child under 16 years did not receive non-UK sourced, virus-inactivated FFP.

An ABO mismatch transfusion could have been prevented by transferring data from the old to the new laboratory computer system as the blood group discrepancy would have been noticed.

The development of IT links between blood transfusion laboratories in different hospitals would significantly reduce the number of cases of IBCT (mainly failure to administer irradiated products) when patients with special requirements are transferred between institutions. In 2006, 12 of the 77 (15.6%) cases of failure to supply irradiated products could have been prevented in this way. (This is unchanged since 2005 when 16% of 'preventable' cases were reported.)

There were 6 cases where red cells were issued inappropriately by electronic selection in contravention of national guidelines and local policies. Four of these led to the issue of red cells incompatible with a known alloantibody. In all

4 cases electronic selection was performed despite a positive antibody screen result. In 1 of these cases the laboratory computer system cannot automatically prevent issue if a positive antibody screen is detected but relies on manual entry of 'not for computer compliant issue'. The other 2 violations involved electronic issue despite inadequate clinical details and issue based on results from a specimen number more than one-year-old (allowed by the computer system). Five of the 6 laboratory staff involved in these cases worked routinely in the laboratory.

Learning points

- Merging of computer records is essential for safe practice. Laboratories should review their procedures and ensure that they have robust procedures for merging of records by appropriately trained and competency-assessed staff. Ultimately, the problem of multiple hospital numbers and case records should be reduced by routine use of the unique NHS Number as a primary patient identifier in line with the recent recommendation from the National Patient Safety Agency[13].
- When laboratory IT systems are 'off-line', non-essential transfusions should be avoided. Robust manual back-up procedures and recovery plans must be in place and tested.
- Laboratory IT systems should be designed to ensure that 'warning flags' are prominently displayed, preferably on the opening screen, and cannot be overridden or bypassed.
- Staff must be trained in appropriate search strategies to ensure that all relevant records are accessed.
- Transfusion laboratories should have direct access to the hospital Patient Administration System and / or pathology results and the ability to review haematology results online (ideally on the same screen).
- When new laboratory IT systems are installed, patient data from the old system should be transferred as a matter of urgency to the new system. Wherever possible this should be done electronically to minimise the risk of transcription errors (see SHOT Annual Report 2005).
- Where historical records were not checked or inappropriate search strategies used, more than 50% involved biomedical scientists who work regularly in the transfusion laboratory. This problem is clearly not confined to 'on call' or rotating staff. Laboratories must ensure that all staff using the IT systems have appropriate training, updates and documented competency assessment.
- Poor communication around the transfer of patients between hospitals remains a significant cause of error. As noted in previous SHOT Annual Reports, the development of IT links between transfusion laboratories, or access to an electronic patient record (EPR) containing accurate and up-to-date transfusion data, would significantly reduce the number of IBCT due to special requirements not being met. This would also impact on delayed haemolytic transfusion reactions caused by blood group alloantibodies that have fallen to undetectable levels. The UK Connecting for Health project has the potential to meet these needs but the question of how and when transfusion data is entered on the EPR must be resolved.
- All laboratories using electronic selection to issue red cells must ensure that their operating procedures are consistent with national guidelines and followed by laboratory staff[14]. The computer algorithms in use must prevent issue outside the guidelines.
- IT systems that support transfusion safety, monitoring and traceability outside the laboratory (e.g. blood-tracking systems and bedside ID systems) should be integrated with laboratory systems and processes. Laboratory staff must be fully trained in relation to these systems and be able to provide support and advice to clinical areas on a 24/7 basis.

Further details of requirements for IT standards and specifications for transfusion can be found in the relevant BCSH and NPSA guidance[15,16].

5.2 Adverse events relating to anti-D immunoglobulin (Ig) (n=77)

Seventy-seven events were related to anti-D immunoglobulin administration and are summarised in table 18 below.

The cases of most concern were those in which administration of anti-D Ig following delivery was delayed or omitted, and those where misunderstanding of antenatal serology resulted in failure to monitor the antibody level appropriately during pregnancy (e.g. case 24 below).

The use of routine antenatal anti-D prophylaxis (RAADP) is increasing as the recommendations of the National Institute for Clinical Excellence (NICE) are being adopted[17]. There is therefore an increase in the number of antenatal samples with low levels of anti-D, presenting laboratories with the problem of determining whether this is passively acquired or immune. The BCSH guidelines for blood grouping and antibody testing in pregnancy provide guidance on appropriate follow-up and further investigation[18].

It should also be noted that administration of anti-D prior to taking the second blood sample at 28 weeks gestation (as recommended by NICE) carries the risk of inappropriate administration if the D group determination at booking was incorrect or a weak D unresolved. Implementation of routine fetal genotyping will mitigate these risks.

Table 18
Cases involving anti-D Ig administration with the site(s) of contributing errors
77 cases, 79 errors

Type of event	Number
Omission or late administration of anti-D Ig *Laboratory errors* *Midwife/nurse errors*	26 7 19
Anti-D Ig given to D pos patient *Laboratory errors (including 8 weak D groups)* *Midwife/nurse errors*	19 12 7
Anti-D Ig given to patient with immune anti-D *Laboratory errors* *Midwife errors*	13 6 8
Anti-D Ig given to mother of D neg infant *Midwife error (anti-D given before cord group done)* *Laboratory error (4 wrong D group determinations, 2 wrong result manually entered onto computer, 2 infants grouped as D neg but anti-D issued in error)*	9 1 8
Anti-D given to wrong patient (all were midwife/nurse errors)	4
Wrong dose given (1 lab error, 1 doctor error)	2
Anti-D Ig expired or out of temperature control *Laboratory error* *Also midwife error* *Clinical error in community*	2 1 1 1
Other (laboratory errors)	2
Total cases ***Total errors***	**77** ***79***

Omission or late administration of anti-D

This was a heterogeneous group of cases. Seven resulted from laboratory errors, including incorrect transcription of the D group of an infant, selection of an incorrect 'standard comment', failure to issue anti-D, failure to recognise the requirement for anti-D in a patient at 19/40 gestation admitted with an antepartum haemorrhage, and 1 difficult case in which the D group was determined as weak D and the patient treated as D positive, including transfusion of D positive blood, but subsequently developed anti-C+D.

In 19 cases the primary error was by a midwife or nurse, 7 occurred in the community and 12 in a hospital setting. In many cases the reason for late or non-administration was not clear. Lack of communication and poor documentation were common features.

These cases highlighted the need for clear protocols and definition of responsibilities within care pathways.

Anti-D Ig given to D positive patients

These cases resulted from errors in D group determination, documentation or communication, or reflected misunderstanding of the laboratory report. Ten involved patients with weak D antigen, and, as commented in previous reports, may be unavoidable, as technologies differ in their sensitivity.

Eight cases of weak D were reported as laboratory errors, but in 2, a change of D status was recorded in the notes but not noticed by the midwife.

In 4 cases, the D group was incorrectly determined by the laboratory as D negative, with 2 being due to problems with laboratory analysers.

Five patients documented as D positive were given anti-D in error, 2 by a community midwife without checking the group, 2 by hospital midwives (in 1 case the wrong patient's grouping result was stuck in the notes), and 1 by a theatre staff nurse following evacuation of retained products of conception.

Anti-D Ig given to patients with immune anti-D

These 13 cases revealed a worrying inability of laboratory staff and midwives, to interpret the finding of anti-D in routine antenatal serological testing. They are of major concern, as misinterpretation can result (as in case 24) in failure to monitor the antibody level during pregnancy, with the risk of missing the development of haemolytic disease of the fetus and newborn. In a further case, classified as 'other', an anti-D found at 28 weeks was assumed to be passively acquired and no further investigation was done.

Laboratory errors

Laboratory errors accounted for 37 (47%) of the reported errors in this section. In total there were 10 D typing errors, of which 2 involved manual tube tests that were incorrectly performed, 3 were errors in manual recording of results from automated / semi-automated analysers and 5 errors were reported due to analyser problems. Three of these cases were from one site that had a software problem on an automated analyser. Such failures should be reported to the manufacturer and to MHRA Medical Devices division so that all users are alerted.

Four laboratory errors, in particular, raise issues of appropriate staffing levels and experience: in 1 case an MLA was responsible for issuing anti-D to a woman who had immune anti-D. Another report stated that there were insufficient experienced staff to interpret a Kleihauer film, hence the Kleihauer was not reported within 72 hours and anti-D administration was delayed. In 2 cases, misinterpretation of antibody identification results by BMS staff meant that appropriate fetal monitoring was not carried out, with possible dire consequences, as discussed above.

Case 24 – misinterpretation of an antibody panel had serious consequences

A D negative pregnant woman suffered an antepartum haemorrhage at 16 weeks gestation and received anti-D Ig. At 28 weeks a strongly positive antibody screen was misinterpreted by the laboratory as being due to prophylactic anti-D, quantification was not done and she received a further prophylactic dose. She went into spontaneous labour at 33 weeks. A full antibody identification panel revealed anti-C+D, with a level of anti-D of 75.4iu/mL. The infant required phototherapy for 5/52 and 3 top-up transfusions. Investigation in the laboratory found that there was no SOP for laboratory testing following administration of prophylactic anti-D, and the laboratory report at 28 weeks had been inappropriately authorised.

Case 25 – anti-D Ig given unnecessarily

A D negative patient known to have alloimmune anti-D since 2003 delivered a D positive infant and was given 500iu of anti-D Ig. This was given by the midwife from stock held on the delivery ward, on receipt of the cord blood group result and without checking the patient's notes. An identical incident involving the same patient had occurred 2 years previously.

It appeared that the standard practice on the unit was to give anti-D Ig to all D negative mothers following delivery of a D positive infant, unless advised to the contrary by the laboratory. This policy has now been changed; stocks of anti-D Ig were withdrawn from all postnatal wards and are now issued from the transfusion laboratory for individual patients, after interrogation of electronic records to ascertain suitability.

Midwife education was also carried out.

Learning points

- Laboratories undertaking antenatal serological testing should have clear protocols based on BCSH guidelines including algorithms for repeat testing in cases where there is uncertainty whether anti-D is passive or immune[18].
- Laboratory reports should provide clear and unambiguous advice on the need for repeat testing and prophylactic anti-D administration.
- Senior, experienced laboratory staff should take responsibility for interpretation of results and issue of anti-D.
- The introduction of RAADP should be supported by education of doctors and midwives (in hospital and primary care) regarding the significance of antenatal antibodies.
- Agreed protocols, compliant with current legislation, should be implemented for the issue and prescription of anti-D Ig.
- Problems with reagents or laboratory equipment should be reported to the manufacturer and to MHRA Medical Devices division so that other users may be alerted. www.mhra.gov.org.

5.3 Summary of laboratory errors

Table 19
Summary of blood transfusion laboratory errors – all cases (where known)

	Total Errors	Wrong sample	Transcription	Interpretation	Component Selection/ issue errors	Labelling	Procedural errors	Testing
Wrong blood – ABO group	7	3	3					1
Wrong blood – Others	20		4		8	5	3	
ABO mismatched transplant	3						3	
Special requirements not met	42				42			
Inappropriate transfusion	0							
Anti-D errors	42		2	10	5		10	15
Unsafe transfusion	13						13	
Other pre-tx testing errors	28 cases 29 errors			1			22 cases 23 errors	5
Total cases (where known)	**155**	**3**	**9**	**11**	**55**	**5**	**51**	**21**
Total errors	**156**	**3**	**9**	**11**	**55**	**5**	**52**	**21**

COMMENTARY

- The 17.5% reduction in reports in 2006, coinciding with the implementation of SABRE and the Blood Safety and Quality Regulations, is of concern, and suggests that there has been under-reporting this year.
- There were 125 cases this year, including 2 with a fatal outcome, in which there was a junior doctor error in requesting and/or prescribing blood (79 cases where special requirements were not met, and 46 where transfusion was inappropriate). See SHOT Recommendations of the Year (p.19), recommendation 1.
- An increasing proportion of IBCT errors arise in hospital laboratories, with a disproportionate number occurring outside of traditional core hours [DA, personal communication]. Some errors are due to basic slips and lapses, and some to lack of knowledge and competence.
- Failure to check the 3 unique patient identifiers on the patient wristband against the blood component label at the patient's side remains a source of error, and contravenes NPSA SPN 14 and NHS QIS Standards [1,7]. In 6/7 cases where the wrong component was taken to the clinical area, and 7/10 cases where the component was given to the wrong patient, the blood was 'checked' away from the bedside against a compatibility form. Many hospitals have successfully eliminated the compatibility form altogether from the bedside check[19]. This is strongly encouraged and is a recommendation of NPSA SPN 14.
- Implementation of an integrated care pathway or care bundle for blood transfusion can support good decision making, facilitate communication and documentation of special requirements and improve the safety of the process.

RECOMMENDATIONS

- As required by the CMOs' Better Blood Transfusion, NHS Clinical Governance framework and NHSLA, hospitals must ensure that all IBCT events are reported to SHOT.

  Action: Trust CEOs

- Blood should only be prescribed by a doctor who has undertaken training in blood transfusion and has been assessed as competent.

  Action: Trust CEOs

- The National Transfusion Laboratory Collaborative aims to improve standards, staffing levels, knowledge, competency and skills in hospital laboratories, and should be supported.

  Action: National Transfusion Laboratory Collaborative, stakeholder professional bodies, Trust CEOs

- Hospitals must comply with the requirements of NPSA SPN 14 or NHS QIS Standards for Blood Transfusion. HTTs should investigate and evaluate options for eliminating the compatibility form.

  Action: Trust CEOs, HTTs, HTCs

- HTTs should investigate and evaluate options for introduction of integrated care pathways or care bundles for transfusion. The NBTCs should facilitate this process.

  Action: HTTs, NBTCs

6. Near Miss Events

Definition

Any event which, if undetected, could result in the determination of a wrong blood group, or issue, collection or administration of an incorrect, inappropriate or unsuitable component, but which was recognised before transfusion took place.

This year Near Miss data were not collected in the same format as previous years. Instead a survey was undertaken that spanned 7 months and all hospitals in the UK were invited to take part. The background to the survey and its results are presented here.

Background

Near Miss events are well recognised to be a good indicator of both strengths and weaknesses in many fields and industries[20]. SHOT has been collecting data on Near Miss incidents in the transfusion process nationally since 2000/2001. The scheme was first piloted in 1998 in 25 hospitals over a 7-month period. A larger survey was carried out the following year, which provided very valuable data and a clear impetus to continue.

In total 4,867 events were collected and reviewed from 1998 to 2005. Because of the large numbers of events seen by hospital staff, questionnaires were designed specifically to be short and simple to fill in. For each event, participants were asked to complete 1 of 5 questionnaires designed for 5 distinct areas of the transfusion process from taking a patient sample to the transfusion at the bedside. Table 20 shows the 5 questionnaire types and table 21 gives the number of Near Miss reports received annually. By far the largest numbers of reports received were errors at the sample taking stage (2,782 of 4,867 (57.2%)).

Table 20

Near Miss questionnaire types used before 2006

1.	Sample errors
2.	Request errors
3.	Lab sample handling and / or testing errors
4.	Lab component selection, handling, storage and issue errors
5.	Component collection, transportation, ward handling and administration errors

Table 21

Numbers of Near Miss reports received annually.

1997/1998 (pilot 1)	**64**	
1998/1999 (pilot 2)	**145**	
1999/2000 (year 1 of national reporting)	**157**	
2000/2001	**452**	188% increase on previous year
2001/2002	**709**	57% increase
2003	**906**	28% increase
2004	**1,076**	19% increase
2005	**1,358**	26% increase & 765% increase since national reporting began
Total	**4,867**	

From November 2005 reporting of all SHOT events, including Near Miss, was transferred to the SABRE electronic reporting system. This increased the workload for the SHOT office and a review concluded that Near Miss reporting in its existing form was of insufficient value to be worthwhile. Existing data have already shown where the majority of Near Miss events take place and there appears to be little or no advantage in continuing to collect data in a way that simply adds numbers without adding information.

While reported Near Miss events are great in number, only 55% of hospitals on the SHOT database sent in reports in 2005. With that in mind the survey was designed to try to determine the true number of incidents occurring.

The Survey in 2006

The survey questionnaire was designed to be simple and quick to use and gave the user the opportunity to complete it at whatever time intervals were suitable for the individual or team concerned. It was built in Microsoft Excel spreadsheet format and simply required the reporter to enter a number against the type of incident seen. No description or text was requested, making the task as effortless as possible. The survey was sent by email to 396 hospitals for whom email addresses were available, together with a set of instructions for use and was to run from 1st June 2006 to 31st December 2006.

Participation

A total of 126 participants returned spreadsheets giving data obtained from 136 hospitals (34.3% return).

Results

The numbers of incidents reported by participants varied greatly (see figure 5). Numbers ranged from 0 to 627. Four reports was the number reported most frequently (13 hospitals), the median was 7 (reported by 5 hospitals) and the mean was 21.4 (reported by 3 hospitals).

Figure 5
Numbers of incidents reported

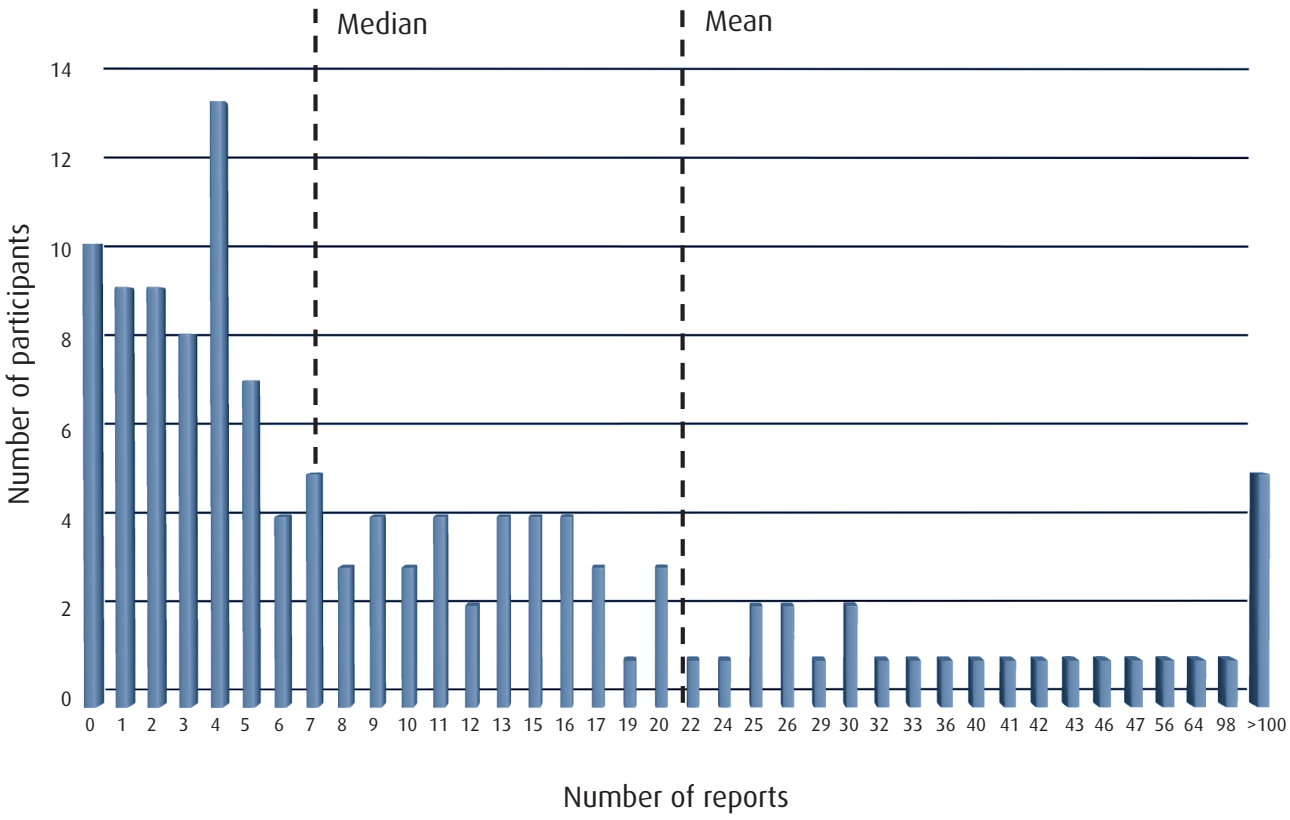
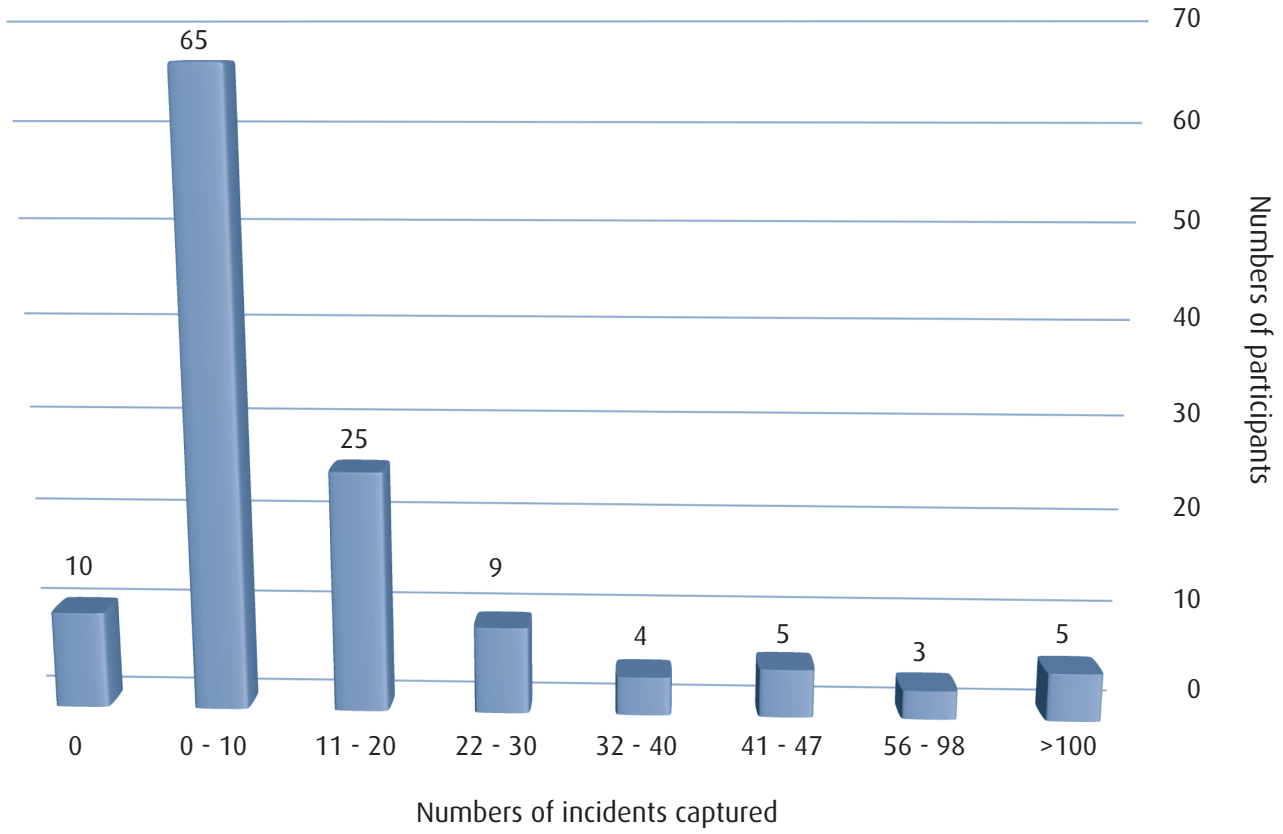


Figure 6
Numbers of incidents reported



The spreadsheet's 4 worksheets carried a total of 20 possible incidents (listed together with the results in table 22). There were some markedly different proportions of incident types from those previously seen in standard Near Miss reporting. Errors at the sampling stage were the most numerous in both event reporting and in the survey but request errors made up 23.2% of incidents in the survey compared with 8.9% of the cumulative Near Miss reporting data. Whilst request errors in the survey rose, errors in the laboratory fell from 21.1% of reported events to 10.8% in the survey.

Table 22
Incident types and the responses received

Sampling	**1.**	Blood in tube incompatible with label details in all respects	279	
	2.	Other	1,063	**1,342**
Request	**1.**	Component requested for wrong patient	30	
	2.	Special Requirements not requested	483	
	3.	Request based on erroneous result	47	
	4.	Wrong component requested	31	
	5.	Other	36	**627**
Collection/Admin	**1.**	Collection	111	
	2.	Storage	187	
	3.	Transportation	35	
	4.	Administration of component	28	
	5.	Other	80	**441**
Laboratory	**1.**	Pre-transfusion testing	50	
	2.	Equipment error or failure	24	
	3.	Labelling	61	
	4.	Result interpretation or transcription	42	
	5.	Special requirements not met	20	
	6.	Selection or issue	39	
	7.	Storage	20	
	8.	Other	36	**292**
				2,702

Conclusion

Since the primary objective of carrying out this survey was to try to establish the number of Near Miss events experienced in blood transfusion in the UK, it is disappointing that the return rate for the survey was only 34%. The true scale of the problem, therefore, is still unknown and this may not be helpful in efforts to decide how best to take Near Miss reporting forward.

What is abundantly clear is that errors at the sampling stage of transfusion are routinely picked up by the vigilance of laboratory staff thus preventing potentially hazardous or lethal incompatible transfusions. Although it is reassuring to know that many of these errors are discovered before transfusion takes place, the survey data, together with previous data collection, underlines the need to address the practice of sample taking at national level.

7. Acute Transfusion Reactions

Definition

Acute transfusion reactions are defined in this report as those occurring at any time up to 24 hours following a transfusion of blood or components, excluding cases of acute reactions due to incorrect component being transfused, haemolytic reactions, transfusion-related acute lung injury (TRALI) or those due to bacterial contamination of the component.

Current Category Definitions

- **Isolated febrile**: rise in temperature >1^{0}C with or without minor rigors and chills.
- **Minor allergic**: skin irritation with or without rash.
- **Anaphylactic/anaphylactoid/severe allergic reaction:**
  Anaphylactic/anaphylactoid reaction: Hypotension with one or more of: rash, dyspnoea, stridor, wheezing, angioedema, pruritus, urticaria, during or within 24 hrs of transfusion.
  Severe allergic reaction: A severe allergic reaction with immediate risk to life occurring during or within 24 hours of transfusion, characterised by bronchospasm causing hypoxia, or angioedema causing respiratory distress.
- **Hypotension:** a drop in systolic and/or diastolic pressure of >30mm Hg occurring during or within one hour of completing transfusion, when all other categories of adverse reactions have been excluded together with underlying conditions that could explain hypotension.
- **TACO (Transfusion-associated circulatory overload):** any 4 of the following within 6 hours of transfusion:
  - Acute respiratory distress
  - Tachycardia
  - Increased blood pressure
  - Acute or worsening pulmonary oedema
  - Evidence of positive fluid balance
- **Febrile with other symptoms/signs:** rise in temperature >1^{0}C, with no features of an allergic reaction, but with one or more of myalgia, nausea, change in blood pressure or hypoxia.

Analysis

Ninety-one completed questionnaires were received, plus 1 initially reported as a haemolytic transfusion reaction. Seven were subsequently withdrawn from analysis; 5 where symptoms were due to the underlying disease, 1 that was a haemolytic reaction and 1 in which a patient died from presumed sepsis following ALI (occurring 8 hours following transfusion).

85 questionnaires were therefore analysed.

Gender 43 males, 42 females

Age Range 3 to 91 years; median 72 years

Major Morbidity

There were no deaths, but there were 4 cases of major morbidity, all related to anaphylactic/anaphylactoid reactions (Imputability level 3). One patient suffered a myocardial infarct during a red cell transfusion and 3 patients arrested during transfusion; 1 receiving platelets, 1 FFP and 1 a red cell transfusion.

Table 23

Components Implicated (85 reports)

Reaction	RBC N = 39	Platelets apheresis N = 11	Platelets buffy coats N = 8	FFP* N = 22	Multiple N = 4	Buffy coats N = 1
Isolated febrile	18	1				1
Minor allergic	3	3	1	3		
Anaphylactic/ anaphylactoid/ Severe allergic	11	5	7	15	3	
TACO	1			1	1	
Hypotension				3*		
Febrile with other symptoms/signs	6	2				
Rate per 100,000 units	2.01	11.2	6.6	8.2		

* With the exception of 1 hypotensive reaction to FFP-SD, the remainder were the result of standard FFP

Isolated febrile and minor allergic reactions

There were 30 reports, as shown in table 23.

Anaphylactic/anaphylactoid reactions

There were 22 cases, including 4 with major morbidity.

Case 1 (RBC)

An 83-year-old male had undergone an endovascular aortic aneurysm repair and a unit of red cells was started at the end of surgery. His pre-transfusion BP was 120/55. Within 15 minutes he complained of skin irritation, became hypotensive with a BP of 40/20 and developed chest and back pain. He received adrenaline followed by a noradrenaline infusion. The following day, his troponin had risen from 0.09 to 2.07and his ECG showed ST elevation, confirming a myocardial infarct.

Case 2 (FFP)

A 69-year-old male was bleeding following a coronary artery bypass graft. He was being treated at an NHS site that relied upon the out-of-hours laboratory service of the main hospital 7 miles away. The local policy is to thaw FFP at the first sign of a major bleed and this was initiated. However, the post-operative bleed responded to surgical measures and the patient required only 2 units of red cells throughout both procedures. Despite this, and without coagulation results being available, the FFP was transfused. After receiving 100mL FFP the patient developed severe bronchospasm, and had a respiratory arrest, but was successfully resuscitated.

Case 3 (PLTaph)

A 46-year-old male with alcoholic liver disease and who had a cerebral haemorrhage and a platelet count of 32 x 10^9/l was transfused with a unit of apheresis platelets. After receiving <10mL component, he developed a widespread urticarial rash and a cardiac arrest but was successfully resuscitated.

Case 4 (RBC)

A 32-year-old female with congenital dyserythropoietic anaemia was receiving the second of a 3 unit transfusion. After 15 minutes she developed pruritis, angioedema and nausea. She was given chlorpheniramine but rapidly became dyspnoeic, lost consciousness, had an unrecordable blood pressure and suffered a respiratory arrest. She recovered following mouth-to-mouth resuscitation and hydrocortisone and went on to receive the third unit uneventfully.

Table 24

Clinical features of remaining 18 cases of anaphylactic/anaphylactoid reactions

Case No.	Component Type	Rash	Angioedema	Dyspnoea O_2 sats (%) where recorded	BP	Impaired conscious-ness or collapse	Interval from starting transfusion in minutes
5	RBC/FFP	√		√	?		10
6	FFP	√		√ 83	60/30		80
7	FFP	√		√	100/60 (30mm Hg drop)		30
8	FFP	√			70/30		5
9	FFP	√		√ 92	97/55 (40mm Hg drop)		60
10	Multiple	√	√		90/60	anaesthetised	<5
11	PC-BC	√	√		50/30	√	15
12	PC-Aph	√			?	√	30
13	PC-BC	√	√	√	75/40	√	15
14*	FFP			√ 65	97/45	√	15
15	FFP	√	√		78/40		30
16	RBC/FFP	√		√ 84	60/30	anaesthetised	?
17	PC-?	√		√ 72	87/52		40
18**	RBC				?		?
19	RBC	√	√	√ 91	90/40		15
20	RBC	√		√ 88	65/40		60
21	FFP	√	√	√ 74	86/53		15
22	RBC	√	√		90/50 (20mm Hg drop)		170

* Classified as anaphylactic/anaphylactoid on the basis of a raised mast cell tryptase (56.2)

** Classified as anaphylactic/anaphylactoid on the basis of wheezing

Investigations

Eleven of the 22 patients with an anaphylactic/anaphylactoid reaction were investigated.

Eight were investigated for IgA deficiency, of which 7 had normal levels and 1 detectable but low levels.

In 4, mast cell tryptase was measured, with 3 found to be elevated.

One case was noted to have HPA antibodies.

Severe Allergic Reactions

Nineteen severe allergic reactions were reported; 5 due to red cells, 7 to platelets and 7 due to FFP.

Table 25
Clinical features of severe allergic reactions

Case No.	Component	Fever	Rigors	Rash	Dyspnoea	Hypoxia	Angioedema
23	FFP			√			√
24	FFP			√			√
25	PC-Aph			√	√		
26	FFP			√	√		√
27	RBC			√	√		
28	PC-Aph			√	√	√	√
29	RBC			√	√		
30	PC-Aph			√	√		√
31	FFP	√		√			√
32	PC-BC			√	√		
33	RBC						√
34	PC-BC	√	√		√ (wheeze)		
35	PC-Aph			√	√		√
36	RBC				√		√
37	RBC	√		√	√		
38	FFP			√	√		
39	FFP	√			√		√
40	FFP			√	√		√
41	PC-BC				√ (wheeze)		

Investigations

Nine out of the 19 patients were investigated.

In 8, IgA levels were measured and found to be normal and 1 of 2 patients for HLA antibodies had a positive result.

Hypotension

Three cases of hypotension were reported during FFP transfusions. One occurred during a plasma exchange for TTP (using SD-FFP) and was accompanied by symptoms of hypocalcaemia, and a second during plasma exchange for HUS.

The third occurred after the transfusion of 100mL FFP over 10 minutes prior to insertion of a pericardial drain in a patient with septicaemia and DIC. The patient's baseline systolic pressure was 70mm Hg on inotropes, but rapidly fell to 40mm Hg during the FFP transfusion.

Transfusion-Associated Circulatory Overload (TACO)

SHOT will study transfusion-associated circulatory overload (TACO) in more detail in future reports. However, three reports from this year fitted well into this category.

Case 42

An 85-year-old lady who was bleeding following an aortic abdominal aneurysm repair had received 2 units of red cells, 1 unit of platelets and 4 units of FFP over 4 hours. Her fluid balance was > 2.5 litres positive, she developed dyspnoea and a tachycardia but a CXR was not performed.

Case 43

A 38-year-old lady had a post-operative haemoglobin of 8.4g/dL and a CVP +4cm, but was nevertheless prescribed 4 units of red cells. The following day she developed dyspnoea and was recorded to have a 7 litre positive fluid balance, to which the unnecessary transfusion had contributed.

Case 44

An 83-year-old lady undergoing an abdominal aortic aneurysm repair received salvaged red cells, 1 unit of allogeneic red cells and 10 units of FFP during surgery. She developed a rash over her abdomen and bilateral lung infiltrates. The FFP had been derived from male donors and the mast cell tryptase (MCT) was normal. Given the volume of components given over a short period, TACO would appear to be the most likely explanation for the CXR changes.

Febrile reactions with other symptoms or signs

An increasing number of febrile reactions have been reported this year due to the blood safety and quality regulations requirement to report these to MHRA. Whilst the majority of patients are either asymptomatic or have rigor and chills, there is a proportion who develop additional symptoms that make the reactions difficult to classify.

Five out of 8 in this group became breathless, in the absence of wheezing or other clinical features of an allergic reaction, and in 4 of these transient oxygen desaturation was evident. Seven of the 8 developed either chest or loin pain or described aching in their limbs. Significant changes in blood pressure were documented in 5 of the 8; 3 of which became hypertensive.

In 4 out of 8 cases, bacterial culture of the unit was not performed.

Table 26
Febrile reactions with additional features

Case number	Dyspnoea (sats%)	Myalgia/ chest pain	Change in blood pressure	Nausea and/or vomiting	Unit bacterial culture	Other Investigation	Time to recovery (hr)
45 platelets	√ 85		Increase		Neg	IgA normal MCT normal	6
46 platelets		√	Increase		Not done	None	0.2
47 RBC		√	Fall		Not done	None	?
48 RBC	√	√		√	Neg	IgA normal	0.5
49 RBC	√ 82	√	Fall	√	Not done		1.5
50 RBC		√	Increase		Not done	HLA antibodies detected	6
51 RBC	√ 72	√		√	Neg		4
52 RBC	√ 87	√			Neg	MCT normal	6

MCT = mast cell tryptase

Paediatric cases

There were 5 reports of acute transfusion reactions in patients aged less than 18. Three were allergic reactions. There was 1 isolated febrile reaction, and there was 1 report of an anaphylactic/anaphylactoid reaction in a 15-year-old patient, who had received appropriate treatment with FFP (case 15 in table 24).

Appropriate use of FFP and platelets

Table 27

Category	Number of patients	Indication given
Indicated	13	3 plasma exchange 1 DIC 4 urgent reversal of warfarin 4 massive transfusion with raised INR 1 intervention with raised INR
Not indicated	9	4 non-urgent warfarin reversal 1 PPH requiring 4 units red cells with normal INR 3 post-operative with normal INR 1 post-operative bleed requiring surgical intervention

Use of FFP

In 9 out of 22 patients, the use of FFP was not justified according to current guidelines (table 27).

Use of platelets

There were 12 reports of anaphylactic/anaphylactoid or severe allergic reactions to platelets, and 2 reports of febrile reactions with other symptoms or signs. In 10 of these cases, platelets were given appropriately. In 2 cases the use of platelets appeared to be outside guidelines, and in 2 cases insufficient information was available.

COMMENTARY

- Acute transfusion reactions continue to be an important and largely unpredictable hazard of transfusion.
- For the second consecutive year, there has been an increase in the number of allergic or anaphylactic/anaphylactoid or severe allergic reactions reported due to red cells. A sustained increase merits investigation by the UK blood services.
- Only one third of the anaphylactic/anaphylactoid reactions occurred within 15 minutes of commencement of the transfusion. This highlights the need for transfusions to be administered at times and in locations permitting careful observation of the patient. Out-of-hours transfusions should be avoided if possible.
- A higher proportion of patients with significant febrile reactions, 18/26 (69%) compared with 9/17 (52%) in 2005, had bacterial cultures performed.
- There is still inappropriate prescription of FFP, particularly with respect to the reversal of anticoagulation.
- The classification of acute transfusion reactions is often problematic and, with increasing reporting, there is awareness that not all of them fall into existing categories. A new classification of transfused reactions has been developed by ISBT, which if fully utilised would allow international comparison of data. It includes several additional categories such as transfusion-associated dyspnoea. Another recent reclassification has included an 'inflammatory' group covering reactions with rigors, myalgia, hypotension and shock in the absence of allergic symptoms[21].
- An elevated mast cell tryptase, as a marker of mast cell activation and degranulation, will confirm an anaphylactic/anaphylactoid or allergic reaction. However a normal result does not exclude these diagnoses. MCT levels should be measured between 15 minutes and 3 hours after the reaction and should be repeated at 24 hours to establish whether levels are returning to baseline[22].

RECOMMENDATIONS

- All prescriptions for blood components must be clinically justified and in line with current guidelines to ensure that the benefits exceed the risks[23,24,25,26].

  Action: Consultant haematologists with responsibility for transfusion should ensure that BCSH guidelines are incorporated into local protocols

- Junior doctors should be educated, trained and competency assessed in transfusion medicine before being permitted to prescribe.

  This is discussed in detail in the Key Message and Recommendations of the Year (pp. 17, 19).

- Anaphylactic/anaphylactoid reactions may occur at any stage during the transfusion, emphasising the need to keep all patients receiving a transfusion visible and accessible to nursing staff. Out-of-hours transfusions should be avoided unless essential.

  Action: Hospital Transfusion Teams

- All serious transfusion reactions must be investigated. Bacterial cultures must be taken in a febrile reaction when the rise in temperature exceeds 1.5°C or the reaction is otherwise sufficiently severe to merit discontinuing the transfusion[12]. An update of BCSH guidelines is in progress.

  Action: Consultant haematologists with responsibility for transfusion should implement current best practice.

8. Haemolytic Transfusion Reactions

Definition

Haemolytic transfusion reactions are split into two categories: acute and delayed. Acute reactions are defined as fever and other symptoms/signs of haemolysis within 24 hours of transfusion, confirmed by a fall in Hb, rise in LDH, positive DAT and positive crossmatch. Delayed reactions are defined as fever and other symptoms/signs of haemolysis more than 24 hours after transfusion, confirmed by one or more of: a fall in Hb or failure of increment, rise in bilirubin, positive DAT and positive crossmatch not detectable pre-transfusion. Simple serological reactions (development of antibody without pos DAT or evidence of haemolysis) are excluded.

Thirty-six questionnaires were received: 1 was transferred to the Acute Transfusion Reaction (ATR) section and another to the IBCT section; 1 was transferred from the ATR section, and 1 was submitted in duplicate.

This section describes the main findings from 34 completed questionnaires: 11 acute and 23 delayed reactions.

Patients

11 males (5 acute, 6 delayed) and 23 females (6 acute, 17 delayed)

Age range 11 months – 92 years

Four reports relate to patients <18 years, and 1 to a patient <12 months. Two, aged 11 months and 5 years, suffered AHTRs following ABO incompatible platelet transfusions (cases A9 and A10). Two, aged 9 and 10, both with sickle cell disease, suffered from DHTRs (cases D4 and D9).

Mortality, morbidity, and imputability

Acute reactions (11)

There was 1 death, in an infant already on ITU, thought to be unrelated to the transfusion reaction. There were no cases of serious morbidity, although 2 patients suffered haemolysis due to ABO antibodies from group O platelets. One required admission from outpatients to the ward.

One reaction was reported as possibly related, 5 as probably related and 5 as definitely related to the transfusion. In 2 cases, where an antibody to a low frequency antigen was found retrospectively, there were definite signs of an acute reaction, but no conclusive evidence of haemolysis. These cases should be interpreted with caution.

Delayed reactions (23)

There were no reports of mortality or major morbidity associated with the DHTRs, and 7 patients were reported to show no clinical signs or symptoms. Two patients were already on ITU, 4 required admission to the ward, and at least 1 required a further transfusion.

Laboratory signs of haemolysis

Many patients showed laboratory signs of haemolysis without any clinical signs being noted. The laboratory signs are often complicated by the underlying disease, and are defined as follows:

- Group 1 with Positive DAT only
- Group 2 Falling haemoglobin(↓Hb)/positive DAT/spherocytes (2 of these parameters)
- Group 3 Elevated bilirubin ± ↓Hb ±positive DAT ±spherocytes
- Group 4 As group 3 + renal impairment

4 patients were in Group 1
6 patients were in Group 2
13 patients were in Group 3

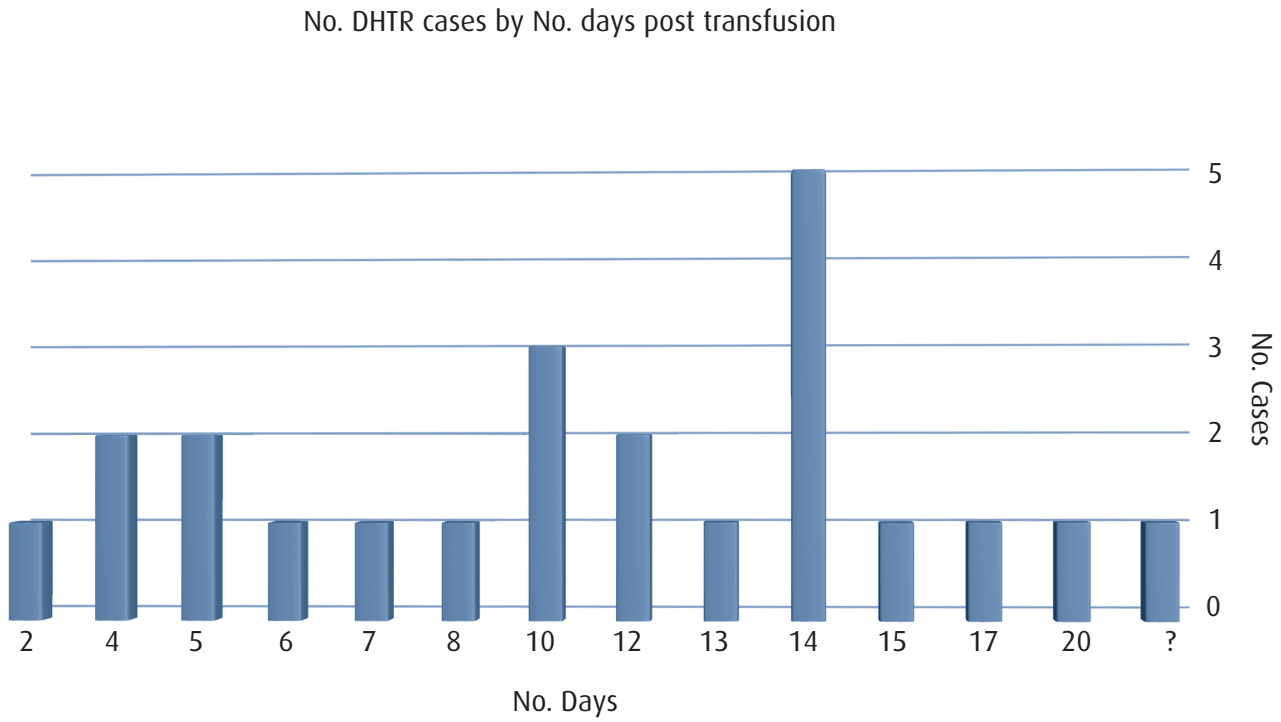
Timing of reaction in relation to transfusion

Acute

Eight reactions occurred during the transfusion, and 3 within 24 hours of the transfusion. One reaction due to a platelet transfusion was reported as occurring 4 days post-transfusion, however the patient received 2 mismatched platelet transfusions on days 1 and 3 and the bilirubin was noted to be raised on day 4 (see vignettes).

Delayed

Figure 7
Time relationship to transfusion



Median = 10 days
Range = 2 to 20 days

Figure 7 shows the reported interval in days between the implicated transfusion and signs or symptoms of a DHTR. The intervals given are not necessarily those when the signs or symptoms were first noted; in asymptomatic cases this relates to the number of days that elapsed before a repeat sample happened to be tested. There was one case where symptoms were noted within 48 hours of transfusion; however, this patient also received a previous transfusion 7 to 8 days before the onset of laboratory signs, which was more likely to have been implicated in the DHTR than the reported transfusion (case D13 – see vignette).

Serological findings

Acute reactions

Two reactions were due to anti-A from mismatched apheresis platelets, despite these being tested and found negative for high-titre anti-A and anti-B. Three occurred in patients where antibodies to low frequency antigens were found retrospectively, following a negative antibody screen and electronic issue of blood: in 1 case the antibody was identified as anti-Wr^a, but in the other 2 cases no specificity was identified, even after referral to IBGRL; in these latter 2 cases the evidence for haemolysis is low or absent. In 2 cases no antibody was detected until several days post transfusion (anti-Jk^b and anti-S+K) and it is unclear whether these were the cause of the reactions. In 1 case a cold agglutinin appeared to be responsible for the acute reaction, although further red cells antibodies developed over the next few days. In 1 case anti-Vel was apparently misidentified as a cold antibody. In 1 case several new antibodies developed, which may have been detectable pre-transfusion had a fresher sample been used. One reaction was caused by an enzyme-only anti-C. Table 28 shows details.

Table 28
Acute reactions – serology and symptoms and laboratory signs (11 cases)

Case No.	Antibody (ies) in plasma	Clinical Symptoms	Laboratory Evidence	Comments
A1	Anti-Jk^{a} + S + ?K	Fever and dark urine	Bilirubin 18 to 64	Pre-existing anti-Fy^{b} + E. Samples taken 2 days later showed additional antibodies.
A2	Anti-Wr^{a}	Fever, chills, rigors, dark urine, jaundice	Poor/absent increment in Hb following transfusion	Electronic issue.
A3	Anti-Jk^{b}	Fever, chills, rigors	Bilirubin 11 to 47 (3 days post-tx)	Anti-Jk^{b} not detectable until 7 days post reaction.
A4	Anti-Vel + Kn^{a}	Chills, rigors, dark urine, hypertension, hypothermia, increased pulse rate	Poor/absent increment in Hb	Thought to be cold antibody though DAT neg. Ab disappeared on prewarming. Anti-Vel identified retrospectively.
A5	Cold agglutinin reactive at 30^{o}C	Fever, rigors, dark urine, jaundice	DAT pos, no other lab results reported	Subsequent txs tolerated through blood warmer. Anti-C^{w} developed 6 days later, followed by anti-E.
A6	Probable unidentified antibody to low frequency antigen	Fever, rigors, back pain, hypotension, tachycardia	DAT neg pre- and post-tx, bilirubin 18 to 36	Screen negative, electronic issue, but unit found to be incompatible retrospectively by IAT.
A7	Anti-Jk^{a} + S + Kp^{a} + Lu^{a} + HI	Dyspnoea/difficulty breathing, anxiety, hypertension & drop in O_2 sats	Bilirubin 9 to 63	Pre-existing anti-E + Rg1. No retrospective testing. Pre-tx sample taken 72 hours instead of 24 hours.
A8	Anti-C (enzyme only)	Fever, rigors	Poor/absent increment in Hb, bilirubin 7 to 95	
A9	Anti-A from group O platelets	Jaundice	Bilirubin16 to 94 to 210	Platelets tested and labeled as 'high titre negative'.
A10	Anti-A from group O platelets	Fever, rigors, headache	Bilirubin 11 to 62, pos DAT	Platelets tested and labeled as 'high-titre negative'.
A11	Unidentified antibody to low frequency antigen	Fever, chills, chest pain/discomfort, rigors	DAT negative, no rise in bilirubin	Screen negative, electronic issue, but unit found to be incompatible retrospectively by IAT.

Delayed reactions

Kidd antibodies were the most commonly implicated, in 15/23 (65%) of cases, either singly or in conjunction with other specificities. Table 29 shows the specificity of new antibodies detected post-transfusion, by blood group system.

Table 29
Delayed reactions – serology and time after transfusion

Case No.	New antibody (ies) in plasma	Antibodies in Eluate	Comments	No. days post-tx
D1	Anti-Fy^{b}	No eluate performed		**20**
D2	Anti-Fy^{a} +M+?	Anti-Fy^{a}	Pre-existing anti-E.	**10**
D3	Anti-D + C	No eluate performed	Retrospective testing detected anti-D in pre-tx sample by solid phase technique only. Cold antibodies detected pre-tx.	**7**
D4	Anti-Fy^{a}+Jk^{b}+M	Anti-Fy^{a}	Pre-existing anti-C+e+K. Required admission.	**12**
D5	Anti-Fy^{a} + Jk^{a}	Anti-Fy^{a} + Jk^{a}	Pre-existing anti-E. Required further transfusion.	**10**
D6	Anti-Jk^{b}	No eluate performed	Pre-existing anti-Fy^{b}. Already on ITU.	**4**
D7	Anti-Jk^{a}	Anti-Jk^{a}		**8**
D8	Anti-Jk^{a}	No eluate performed		**10**
D9	Anti-Jk^{b}	No eluate performed	Required admission.	**14**
D10	Anti-Jk^{a} + enz-only anti-E	No eluate performed	Patient already on ITU.	**5**
D11	Anti-Jk^{b}	No eluate performed	Pre-existing anti-E. Required admission.	**13**
D12	Anti-Fy^{a} + E	Anti-Fy^{a}	Pre-existing anti-K.	**4**
D13	Anti-Jk^{a} + f + M + s	No eluate performed	Pre-existing anti-K.	**2 – 9**
D14	Anti-E	No eluate performed		**14**
D15	Anti-Jk^{a}	No eluate performed		**15**
D16	Anti-Jk^{a}	Anti-Jk^{a}		**17**
D17	Anti-Jk^{a}	No eluate performed	Pre-existing anti-Fy^{b}.	**14**
D18	Anti-S+Jk^{a}+Fy^{a}+E		Known to NBS.	
D19	Anti-Fy^{b} + c	Anti-Fy^{b} + c		**12**
D20	Anti-E	No eluate performed		**14**
D21	Anti-Jk^{a}	No antibodies detected		**6**
D22	Anti-Jk^{a}	No eluate performed	Pre-existing anti-e. Admission required.	**8**
D23	Anti-C	No eluate performed	AIHA.	**14**

Table 30
DHTRs – New specificities by blood group system

Antibody specificity by blood group system	Number of cases	Sole *new* antibody
Kidd		
Jk[a]	11	7
Jk[b]	4	3
Rh		
D	1	0
C	2	1
E	5 (1 enz only)	2
c	1	0
f	1	0
Duffy		
Fy[a]	5	0
Fy[b]	2	1
MNSs		
S	1	0
s	1	0
M	3	0

Serological Techniques Used – DHTRs only

Table 31 shows the technology used for antibody screening by IAT.

Table 31
IAT technology used for antibody screening

IAT screening technology	Number of cases	By automation
DiaMed	10	9
BioVue	2	2
Solid phase	2	2
No answer	10	10

In 13 cases plasma was used for pre-transfusion testing, and in 1 case serum (9 not stated).

Fifteen undertook an IAT crossmatch, and 6 electronic issue; 2 did not answer the question.

Use of eluates

Eight out of 23 (35%) stated that an eluate made from the patient's post-transfusion red cells was tested for antibody; 5/8 were performed in reference labs and 3 in-house. In 7 cases a specific antibody(ies) was identified. In 1 case the eluate was negative.

Retrospective testing findings

Retrospective testing of the pre-transfusion sample was undertaken in 11/23 (48%) cases; the same result was obtained in 10 of these. In 1 case (case 3), the causative antibodies were detectable retrospectively but only by a reference laboratory with a solid phase technique (Capture RRS).

Clinical management and review

Thirty-two (94%) of cases were referred to the HTC, and 22 (63%) to the Transfusion Centre Reference Laboratory. Twenty of these were reported to both.

Vignettes AHTRs

Case A1

An 82-year-old female patient with MDS required a routine top-up transfusion. The patient was found to have anti-Fy^{b}+E antibodies. Compatible antigen negative blood was issued on Thursday evening. On Friday morning the SHO reported the patient as having pyrexia and 'blood' in the urine. Transfusion reaction investigations were carried out using the pre- and post-transfusion samples. No additional antibodies/incompatibilities were observed, but the bilirubin rose from 16 to 64 mol/litre. A further request for blood and a new sample was sent on Saturday and compatible E-, Fy(b-) units were issued. The patient once again developed pyrexia and blood in the urine. New samples were obtained on Monday and referred to the BTS. Anti-Fy^{b} + E + Jk^{a} + S +??K were reported as being present in the plasma. The Hb increased from 6.9 to 9.9 following the first transfusion on Thursday but dropped back down to 6.8 by Monday. Antigen negative blood was transfused with no further problems.

Case A2

A 58-year-old male patient with MDS and no detectable red cell antibodies, received a routine top-up transfusion, issued electronically. The patient experienced fever, chills & rigors after 200 mL had been transfused. Transfusion was stopped and the unit was returned to the blood bank with fresh blood samples. Investigation revealed that although the antibody screen was negative, the implicated unit was incompatible with both pre- and post-transfusion samples, and the post-transfusion sample showed a positive DAT. Anti-Wr^{a} was identified by the BTS reference laboratory. The bilirubin rose from 18 pre-transfusion to 110 post-transfusion, and the Hb fell to below pre-transfusion levels. The patient also suffered from haemoglobinuria, but had no prolonged ill effects.

Case A3

An 86-year-old female patient with no detectable red cell antibodies received a routine 3 unit red cell transfusion for anaemia. The first 2 units were transfused uneventfully, but after 150 mL of the third the patient suffered developed a fever, chill and rigors. The transfusion was discontinued and returned to the laboratory. Retrospective testing on the pre-transfusion sample and tests on the post-transfusion samples still revealed no red cell antibodies, and the DAT was negative; however the bilirubin rose from 11 pre-transfusion to 47, 3 days post transfusion. A sample taken 7 days post transfusion revealed the presence of anti-Jk^{b}. The units transfused were not typed for Jk^{b}. The only sign of haemolysis was an increase in bilirubin 3 days post-transfusion, and this was reported as being possibly related to the transfusion.

Case A4

A 78-year-old male patient with a peri-prosthetic femoral fracture and a history of pernicious anaemia required blood for theatre. The antibody screen was positive and 2+ reactions were noted with all panel cells tested by IAT and stronger reaction by enzyme IAT; the auto was negative. The operation was postponed and samples sent to the BTS reference laboratory. A cold agglutinin was reported and blood compatible when tested strictly at 37°C was issued. The patient received a total of 6 units pre- and during surgery, with no signs of a reaction. Ten days later the patient's Hb was 6.8 and 3 more units were issued as suitable (compatible at 37°C), although the strength of reaction of the antibody had increased to 4+ by IAT. The patient suffered from chills and rigors, and a pyrexia developed during the first unit. The haematologist recommended giving the other 2 units through a blood warmer, after the patient had stabilised. The next day, unit 2 was transfused through a blood warmer, but the patient started shivering after 10 minutes; the transfusion was stopped and the bag returned to the laboratory; dark urine was also noted. Samples were referred to IBGRL and anti-Vel + anti-Kn^a were identified; the DAT was still negative. Laboratory tests showed a small rise in bilirubin, a significant increase in creatinine and a fall in haptoglobins, indicating haemolysis and deteriorating renal function.

Vel antibodies are predominantly IgM (but may also be IgG or have an IgG component) and bind complement; they are well known to cause often severe haemolytic transfusion reactions, may have a wide thermal range and may be reactive by direct agglutination. There has been a previous report of anti-Vel disappearing in vitro on pre-warming[27].

Case A5

A transfusion-dependent, 60-year-old male patient receiving a Stem Cell Transplant for AML received a routine top-up transfusion of red cells. Pre-transfusion testing showed the presence of cold agglutinins with an upper thermal range of 30°C; no antibodies were detected when the testing was undertaken at 37°C. The blood was transfused cold and he developed fever and rigors after 200 mL of the first unit, when the transfusion was immediately stopped. Dark urine and jaundice were also noted. The DAT was weakly positive (both IgG and C3 coating), and the eluate gave non-specific reactions. Subsequent transfusions were given through a blood warmer and were tolerated. Six days after the first transfusion anti-C^w developed, and this was followed by anti-E.

Case A6

A 37-year-old female patient with upper GI bleeding had 3 units of red cells issued electronically following a negative antibody screen. After 100 mL of the third unit the patient suffered from pyrexia, rigors, lumbar pain, hypotension and tachycardia. The transfusion was stopped and the bag returned to the laboratory. The antibody screen and DAT were negative on both pre- and post-transfusion samples, but the unit was incompatible by IAT on both. The bilirubin increased from 18 to 36, but no other laboratory signs of haemolysis were noted. Despite testing against several low frequency antigens no specificity was determined by the reference laboratory.

Case A7

A 44-year-old male patient with haemorrhagic effusion of his right lung, required transfusion. Anti-E plus anti-Rg^a were identified by the BTS reference laboratory and 2 units of compatible blood were transfused. Seven days later 2 further crossmatch compatible units were transfused, but the patient complained of SOB and tachycardia following completion of the second unit, and became jaundiced the next day. A 3-day-old sample was used for the second set of serology and no retrospective testing was possible, since there was no sample left. A post-transfusion sample revealed the presence of anti-S + Jk^a +Kp^a +Lu^a + HI, in addition to the anti-E and –Rg^a. The DAT was positive (C3 coating only), but no antibodies were detected in an eluate.

This reaction might have been prevented had a fresher sample been used as recommended in the BCSH guidelines[28].

Case A8

A multiply transfused 68-year-old female patient developed fever and rigors during a routine transfusion for anaemia. Laboratory testing showed a rise in bilirubin from 7 to 95, and haemoglobinuria was noted. Pre- and post-transfusion samples gave a negative antibody screen, but an enzyme only anti-C was identified by the reference laboratory, in the post-, but not the pre-transfusion sample.

Case A9

An 11-month-old male A D negative infant undergoing cardiac surgery required a platelet transfusion. The patient was given group B negative apheresis platelets on day 0, and group O apheresis platelets on days 1 and 3 (tested negative for high-titre haemolysins), as group A platelets were unavailable. On day 4, laboratory tests showed evidence of haemolysis – raised bilirubin (16 pre, 94 day 1 and 210 day 4); the DAT became positive and anti-A was eluted from the red cells. The patient was already on ITU and died from underlying disease.

Case A10

A 5-year-old female, group AB D positive child with ALL required platelet and red cell transfusion. One unit of group O apheresis (tested negative for high-titre haemolysins) was transfused followed by 1 unit of group A red cells. One hour (68 mL) into the red cell transfusion, the patient developed a fever, rigors and headache. The DAT was positive, the bilirubin rose from 11 to 62, and the Hb fell from 6.7 to 6.1.

Case A11

Following a post-partum haemorrhage, a 36-year-old patient required 4 units of red cells, which were issued electronically. On transfusing the first unit, the patient experienced pyrexia, headaches, shivering, flushing, rigors and tachycardia. The transfusion was stopped. By this point the patient had received all of the unit. The pack, transfusion set, first sample of urine and a new sample for antibody testing were sent to the transfusion department. On retesting of samples, the pre- and post-antibody screens were still negative but the implicated unit was incompatible by IAT on both pre and post samples. This was confirmed by IBGRL to be an antibody to a low frequency antigen, but no specificity was determined. There were no clinical signs or laboratory evidence of haemolysis – the DAT was negative and the bilirubin level remained normal.

Learning points

- If used inappropriately, prewarming techniques can reduce or remove the activity of clinically significant antibodies, and should only be used where cold autoantibodies or specific cold alloantibodies have been positively identified.
- Blood warmers should be used where high-thermal range cold agglutinins are present.
- Some transfusion reactions may be prevented in recently transfused patients, by using fresher blood samples, taken in line with BCSH recommendations[28].
- Group O apheresis platelets can cause acute haemolytic reactions even when tested and found negative for high-titre haemolysins. They should only be used for non-group O patients (particularly paediatric patients) as a last resort, and should not be kept by hospitals as stock.

Vignettes DHTRs

Case D3

An 88-year-old female patient with a GI bleed and no known history of transfusion required red cells during on-call hours. The patient was grouped as O D negative with a positive antibody screen. Cold agglutinins were suspected and the sample was referred to the reference laboratory, where the presence of cold agglutinins only was confirmed. The patient was transfused with 2 units of O D negative blood, followed by 5 units of O D positive blood. Seven days later a further transfusion was required and anti- D+C was identified in the plasma. The DAT was negative and tests indicated that no D positive cells remained in the circulation; the bilirubin was slightly elevated (39) and the Hb dropped from 13.0 immediately post transfusion, to 7.3, initially attributed entirely to continued bleeding. Retrospective testing of the pre-transfusion sample confirmed no alloantibodies by routine techniques (including enzymes), but anti-D+C were identified using a Capture R solid-phase technique.

Case D13

A 68-year-old female patient with known anti-K was transfused with 9 units of K- blood for a massive GI bleed. Six days later, a further 3 units of K- blood were transfused, using a fresh sample for crossmatching. Another 2 days later the patient was noted to be jaundiced with a bilirubin of 130 (pre-transfusion bilirubin not known). The Hb fell to 6.2, from a pre-transfusion Hb of 8.2. Anti-K+Jk^a+s+f+M were identified by the reference laboratory; the DAT was positive with both IgG and complement coating but elution was not performed.

This was reported as a DHTR to the second transfusion 2 days previously. However, it is more likely due to the first transfusion 8 days earlier or to both, since the Hb dropped to below pre-transfusion levels.

Case D18

An 87-year-old female patient with unknown transfusion history required transfusion for anaemia. Anti-K was identified in the pre-transfusion sample and K- blood was transfused. An unspecified number of days later a further sample was tested and multiple antibodies were found. Samples were sent to the BTS reference laboratory where the patient was previously known to have anti-S+Jk^a+Fy^a+E. Fortunately, although this patient had a positive DAT, there were no apparent signs of a DHTR.

Case D23

A 69-year-old male patient with Waldenstrom's macroglobulinaemia and warm AIHA was admitted with an Hb of 7.3g and 2 units of red cells were requested. No underlying alloantibodies were demonstrated and 2 units of blood compatible with the absorbed plasma were transfused. Seventeen days later the patient presented with a Hb of 5.3 and a raised bilirubin of 63 (no pre-transfusion bilirubin available). Allo-anti-C was identified by a reference centre, but no elution was performed.

It is not clear whether the haemolysis was due to the transfusion or the underlying AIHA. However, the laboratory has since implemented a policy to give Rh matched red cells to patients with AIHA.

Learning points

- It is advisable to provide Rh and K matched blood to patients with AIHA, in line with BCSH guidelines[28].

COMMENTARY

- An example of anti-Vel was mistaken for a cold antibody and removed by pre-warming[27].
- Three cases of acute reaction occurred where antibodies to low frequency antigens were undetected in pre-transfusion testing (antigens absent from the screening cells and blood issued electronically). Although reported as AHTRs, only the case involving anti-Wr^a demonstrated a clear haemolytic reaction. Patients may have symptoms of an acute reaction following transfusion of a unit to which they have an antibody, but unless there is evidence of haemolysis, these two facts are not necessarily related.
- Anti-Wr^a is a relatively common antibody and may be naturally occurring; although this antibody can cause severe HTRs and HDN, many examples are of no clinical significance.
- Group O apheresis platelets, which test negative for high-titre haemolysins may cause haemolytic reactions particularly in paediatric patients.
- In all cases but one (where an answer was given) plasma rather than serum was used for both pre- and post-transfusion investigations. It is known that weak complement binding antibodies, e.g. some examples of anti-Kidd, may be missed when using plasma, unless more sensitive techniques are used, e.g. enzyme IAT.
- Only 35% of investigations included testing an eluate made from the patient's red cells. Where a mixture of antibodies is present, an eluate may help to distinguish which specificity(ies) is more likely to be implicated in a haemolytic reaction. Furthermore, the implicated antibody may only be present in an eluate. Identification of all specificities present is essential if further haemolytic reactions are to be prevented.
- As in previous years, communication problems have contributed to DHTRs, where information about previously known antibodies has not been available at the time of a subsequent transfusion.

RECOMMENDATIONS

- Group identical platelets should be selected whenever possible, with group O being the last choice for non group O recipients. Where children are concerned the Amendments and Corrections to the BCSH guidelines 'Transfusion Guidelines for Neonates and Older Children', should be followed[29,30].

  Action: Hospital transfusion laboratories

- Investigation of a suspected HTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. Consideration should also be given to requesting clotted samples for investigation of suspected HTRs and using polyspecific AHG. Where hospital resources are limited, this will require referral to a reference centre.

  Action: Hospital transfusion laboratories

Carried over from 2005:

- All cases of suspected AHTR and DHTR should be appropriately investigated, and ideally referred to a reference laboratory. Referring hospitals should make it clear to reference laboratories that they are investigating a DHTR to ensure that timely, appropriate tests are undertaken. Clinical details should be completed on the request forms and the donation numbers of the units transfused should be included, so that their phenotype can be determined.

  Action: Hospital transfusion laboratories and blood services reference laboratories

- Reference laboratories should ensure that investigation of DHTRs includes testing an eluate made from the patient's red cells when the DAT is positive.

  Action: Blood services reference laboratories

- In line with recommendations made in the BCSH Guidelines consideration should be given to issuing antibody cards or similar information to all patients with clinically significant red cell antibodies[28]. These should be accompanied by patient information leaflets, explaining the significance of the antibody and impressing that the card should be shown in the event of a hospital admission or being crossmatched for surgery. Laboratories should be informed when patients carrying antibody cards are admitted.

  Action: The CMO's NBTC and its counterparts in Scotland, Wales, and Northern Ireland

- There is a need for a review, co-ordinated by a professional national body, of how long specimens should be kept post-transfusion. The review needs to consider the relative risks and benefits of storing specimens beyond the time that they are suitable for use in further crossmatching tests.

  Action: BBTS and BCSH

9. Transfusion-Related Acute Lung Injury

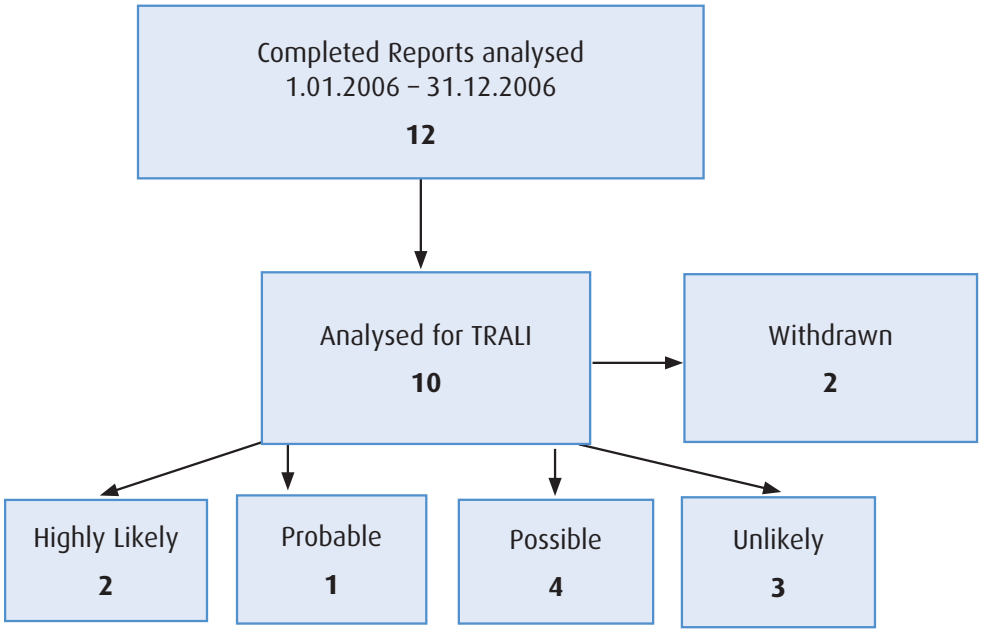
Definition

Acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, not due to circulatory overload or other likely cause.

Twelve case reports of suspected TRALI were received in this reporting year. Of these, 2 were subsequently withdrawn, 1 by the reporters because the reaction was attributed to circulatory overload; the other case did not fulfil the SHOT definition for TRALI because no CXR changes were demonstrated.

Ten cases were analysed, and the assessed probability of TRALI is shown in Figure 8. Two patients died, 7 suffered short-term major morbidity with full recovery and one had long-term morbidity. Of the 2 patients who died, death was probably due to TRALI (imputability 2) in 1 case that had been assessed as highly likely to be TRALI, and death was unlikely to be related (imputability 0) in one 1 that had been assessed as possible TRALI.

Figure 8
Summary of cases



Assessment of TRALI reports

TRALI is a difficult diagnosis to make because there is no specific diagnostic test for this condition and it is easily confused with other causes of acute lung injury, cardiogenic pulmonary oedema and circulatory overload. If the clinical picture occurs in a previously fit patient and relevant leucocyte antibodies are found, the diagnosis is straightforward. Often however, it occurs in patients who have other risk factors for the development of Acute Lung Injury (ALI) or Acute Respiratory Distress Syndrome (ARDS). When TRALI is suspected, a detailed assessment of the clinical event is required together with investigation of the patient and donors. Early discussion with the Blood Service is recommended and blood samples (EDTA and clotted) from the patient should be sent promptly to a Blood Service Reference laboratory. Clinical factors that were taken into consideration in the assessment of cases included: time between transfusion and respiratory deterioration; radiological features; possibility of infection; other risk factors for ALI/ARDS; evidence of circulatory overload and/or impairment of cardiac function; pre-existing cardiac, pulmonary or other disease; and time to respiratory recovery with supportive treatment. Fluid balance in previous 24-48 hours was assessed when possible.

Results of TRALI investigations may not be definitive. Because of the frequency of leucocyte antibodies in the donor population, donor antibodies would also be found in many uneventful transfusions if they were similarly investigated. In an

NBS study of 1166 female donors, HLA antibodies were found in 14.5% (personal communication, Dr S. MacLennan).

The likelihood of TRALI has been assessed in each case. Two intensive care specialists and a transfusion medicine expert (TRALI Expert Panel) have initially assessed all cases reported to the NBS in 2006 (9 of 10) before serological investigation. A transfusion medicine specialist, who has also reviewed cases for the previous three years, has subsequently assessed all cases with the results of TRALI investigations. Reports were finally graded on the basis of both clinical features and laboratory results. Complete results of relevant serological investigations were not available in 2 cases. These cases were not investigated for TRALI following advice from the expert panel.

As in previous years, cases were divided into four groups: 'Highly likely' where there was a convincing clinical picture and positive serology; 'Probable' where there was either a less convincing history and positive serology or a good history and less convincing or absent serology; 'Possible' where either the clinical picture or serology was compatible with TRALI, but other causes could not be excluded; and 'Unlikely' where the picture and serology were not supportive of the diagnosis (see figure 8).

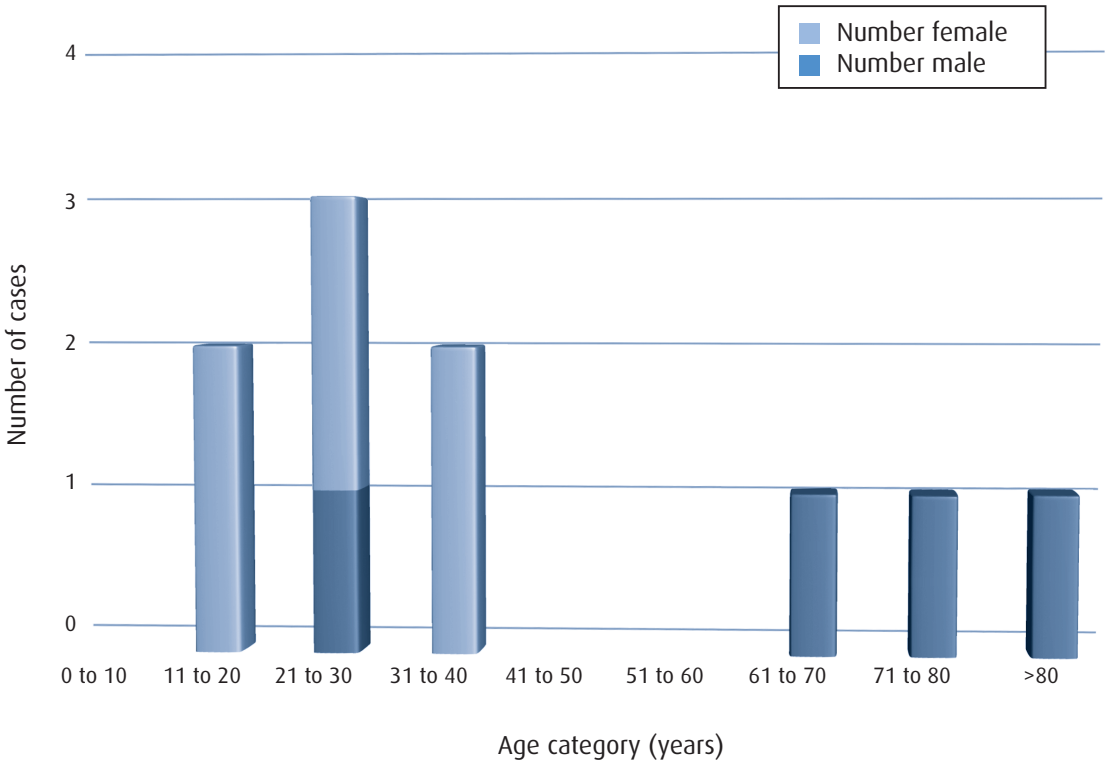
Cases have also been separately assessed by the same SHOT analyst for probability of TRALI according to the American–European consensus definition for comparative purposes. Consensus panel views and recommendations relating to TRALI definition, pathogenesis, investigation, donor management and risk reduction were agreed at an international conference in 2004. These were based on panel assessment of evidence presented by experts (evidence level 3 / 4, grade D) TRALI was defined according to the clinical history and features of cases excluding the results of donor investigations[31]. TRALI was defined as acute onset ALI during or within 6 hours of transfusion with no evidence of left atrial hypertension due to circulatory overload, no pre-existing ALI and no temporal relationship to an alternative risk factor for ALI. Possible TRALI was defined as ALI, with no pre-existing ALI, during or within 6 hours of transfusion with a clear temporal relationship to an alternative risk factor for ALI.

Website tables

Summarised information is presented in this chapter. Data extracted from individual TRALI questionnaires and laboratory results for each case have been tabulated and are available on the SHOT website, www.shot-uk.org.

TRALI Table 1 Patient and component details and patient characteristics
TRALI Table 2 Clinical characteristics and radiological features of cases reported as TRALI
TRALI Table 3 Treatment, investigation results and likelihood of case being TRALI

Figure 9
TRALI reports analysed according to age and sex



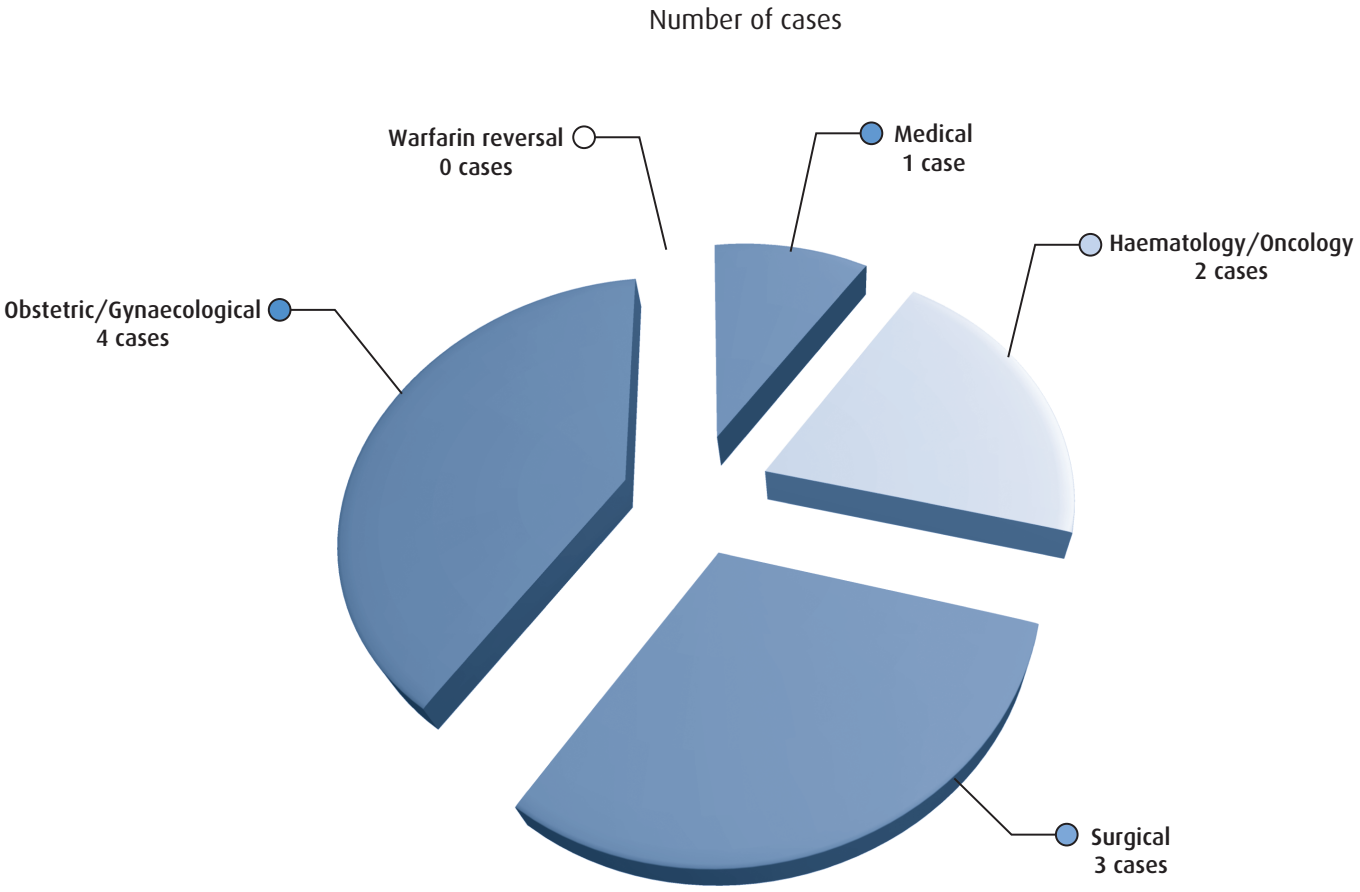
Age and sex

An analysis of cases by age and sex is shown in figure 9. Cases of suspected TRALI were reported in patients aged from 16 to 83 years. Two patients were under 18 years of age. There were 6 female and 4 male patients. Analysis of 193 suspected TRALI cases, of known sex, reported to SHOT from 1996 to the end of 2006 shows a slight excess in female patients (105 cases, 54%) compared with males (88 cases, 46%). Analysis of 156 cases reported to SHOT between 1999 and 2006 for which the probability of TRALI has been assessed gives the same overall proportions (female patients 84 cases, 54%; and males 72 cases, 46%). Analysis of the group according to sex and probability shows a slight excess in males in the highly likely and probable categories (Males 40 cases; 53%; females 36 cases, 48%) and an excess of women in the possible or unlikely cases. (Females 48 cases, 60%; males 32 cases, 40%).

Clinical speciality/diagnosis

Reports have been analysed according to the reason for transfusion (figure 10). The most frequent speciality was Obstetrics and Gynaecology (4 cases, 40%), then non-gynaecological surgery (3 cases, 30%). Haematology/Oncology Departments contributed only 2 cases (20%); one of these reports followed the use of FFP to correct coagulopathy following plasma exchange in a patient with Waldenstrom's macroglobulinaemia (Case 1). Only one medical case was reported. There were no reports of TRALI following warfarin reversal this year. The number and the proportion of haematology/oncology cases are less than seen previously. Fifty-nine of 162 (36%) suspected TRALI cases analysed between 1998 and 2005 occurred in haematology or oncology patients.

Figure 10
Clinical speciality/diagnosis



Clinical features

Clinical presentation

Details of all reported cases are tabulated in TRALI Table 2 on the SHOT website, www.shot-uk.org.

All suspected cases were reported to have been dyspnoeic or tachypnoeic and hypoxic. Eight patients (80%) were treated in ITU and of these 2 were already on ITU before the event; all required mechanical ventilation. Fever was reported in only 1 patient, it was absent in 8 and not recorded in 1. The patient with fever had serological support for immune TRALI but also had a non-ST elevation myocardial infarct (MI) (Case 2). Hypotension was reported as part of the reaction in 3 cases, absent in 6 and not reported in 1. Two of the cases with reported hypotension had immune support for the diagnosis. One of these was again the patient who also had evidence of MI. Signs of heart failure were absent in the 9 cases for whom this was recorded.

Patient outcomes

Details of all reported cases are tabulated in TRALI Table 3 on the SHOT website www.shot-uk.org.

Two patients died: one was assessed as highly likely to be TRALI and the reporter considered that the death was likely to be related to transfusion (imputability 2); the other patient who died was assessed as unlikely to be TRALI and the reporter considered his death to be unrelated to transfusion (imputability 0). The majority of patients (7) made a full recovery from the episode. One patient suffered long-term morbidity from a simultaneous MI that the reporter thought was caused by his TRALI reaction. His respiratory symptoms had fully resolved by the following morning.

Laboratory results

Details of all reported cases are tabulated in Table 2 on the SHOT website, www.shot-uk.org.

All cases were referred to the BTS for investigation and 8 of 10 cases were subsequently investigated at Reference Laboratories. Complete TRALI investigations were achieved in 7 of these cases. In the eighth case, a repeat sample was required from the patient to assess donor antibody concordance but the patient had died. Laboratory investigations were not undertaken in 2 of the 10 analysed cases following advice from the National Expert Panel; one of these had involved large volume transfusion in a patient with severe skeletal thoracic compromise and the other case was assessed as being much more likely to be due to circulatory overload.

Donor antibodies

All donors in whom relevant antibodies were identified were female. In general, untransfused males were excluded from investigation. Transfused males were routinely investigated but none was identified with relevant antibodies. Individuals who have been transfused since 1980 have been excluded from donation since 2004.

Relevant donor leucocyte antibodies (i.e. donor HLA or granulocyte antibody corresponding with patient antigen) were found in 3 of 7 (43%) complete case investigations this year. This is a similar proportion to that in 2005 when these were found in 6 of 16 (37.5%) complete case investigations. A much higher proportion of positive investigations has been found in previous years. Relevant antibody was found in 12 of 17 complete investigations (70%) in 2004 and 21 of 30 (70%) in 2003. The marked reduction in the proportion of cases with relevant antibodies found in the past 2 years is most likely to be due to the policy of using male donor plasma preferentially for FFP and the plasma contribution to platelet pools.

This year 2 cases were associated with donor HLA antibodies corresponding with the recipient and 1 case with concordant donor HNA antibodies (HNA-1a). One of the HLA antibody associated cases (Case 1) involved cryoprecipitate from 2 donors each with HLA antibodies that matched the recipient; 1 had matching HLA Class II antibodies (HLA-DR4 and DR53) and the other had matching HLA Class I antibodies (HLA-B42). The donor in the second case had corresponding HLA Class II antibody (HLA-DR4).

In a further case, a non-specific granulocyte antibody was found in a donor of red cells in OA but it could not be established whether the antibody matched the patient because a fresh sample was required for crossmatch and the patient had died. Multiple alternative risk factors for ARDS were also present in this case.

Patient antibodies

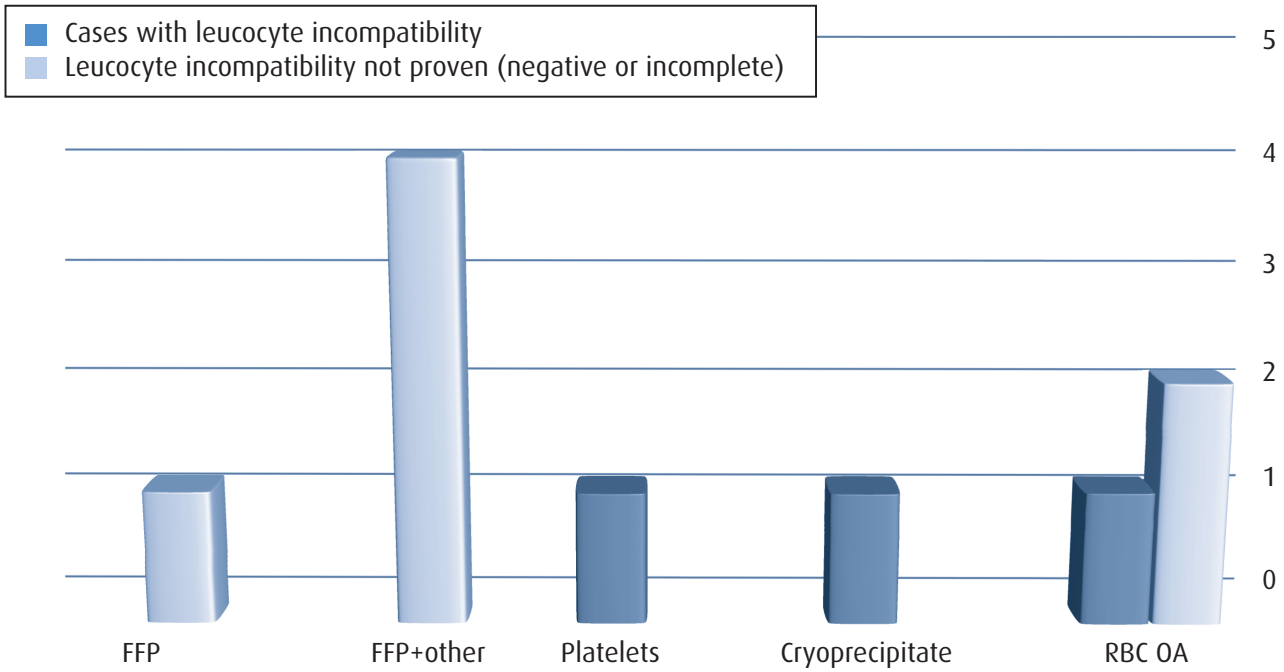
Leucocyte antibodies were found in 2 patients, both had HLA antibodies. In 1 case the antibodies corresponded with 3 of the donors but in this case 1 of the donors had HNA-1a antibodies that matched the patient. In the second case the patient antibody did not correspond with 1 donor but the other donor was not typed. Investigations for patient HLA or granulocyte antibodies were negative in 6 cases and 2 patients were not tested. It is generally considered unlikely that patient leucocyte antibodies have relevance to TRALI pathogenesis when leucodepleted components are transfused. All components, other than granulocytes, have been leucodepleted in the UK since late 1999.

Components

Details of all implicated components are tabulated in TRALI Table 1 on the SHOT website, www.shot-uk.org.

The implicated components in the 3 cases with proven relevant leucocyte antibodies were 2 units of cryoprecipitate in 1 case (2 different donors each with matching antibodies), red cells in optimal additive (OA) in another, and apheresis platelets (2 adult doses from the same donor) in the third case. No case was found involving FFP containing a relevant antibody.

Figure 11
Components transfused in TRALI cases with and without relevant donor antibodies



Comparative results

Preferential use of male donor plasma

In late 2003 the English National Blood Service (NBS), which provides more than 80% of UK blood components, introduced a policy of using male donors as far as possible to produce FFP and plasma for suspension of buffy coat derived platelet pools. The intention of this policy was to reduce the risk of TRALI. Previously issued FFP from female donors was not withdrawn when the policy was introduced. The Scottish National Blood Transfusion Service (SNBTS) followed closely with male FFP in January 2004 and with male plasma for platelet pooling in November 2004. The Welsh Blood Service (WBS) moved to male FFP before January 2005 and male plasma for suspension of buffy coat pools in January 2005. The Northern Ireland Blood Transfusion Service (NIBTS) moved to male donor FFP from April 2004.

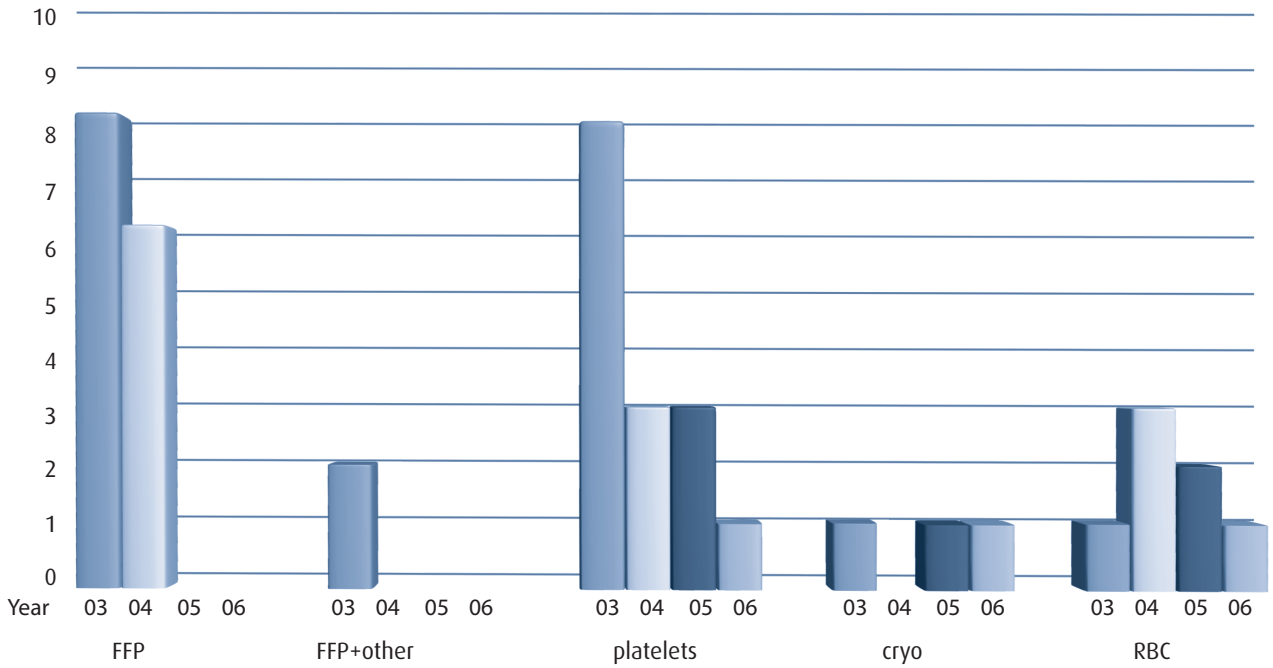
In 2006, the National Blood Service produced 86% of its FFP and 86% of the platelet pools using plasma from male donors; the WBS achieved 100% male FFP and 100% male plasma for platelet pooling as did SNBTS in the same period. The NIBTS produced 100% FFP and > 95% platelet pools using male plasma in 2006. The WBS has also routinely screened female and transfused male apheresis donors for HLA class I and class II antibodies. The NBS does not currently screen apheresis donors for HLA antibodies; approximately 70% of apheresis platelet donors in the NBS are male. The NBS is planning to move to overnight hold of blood donations at 20°C before FFP production. This should make it possible to achieve 100% male plasma for FFP and platelet pools.

Comparison of TRALI reports in 2006 with those in previous years is presented here to assess whether there have been changes in TRALI related events since the change to preferential use of male plasma. There are several confounding factors, which are relevant to interpretation of these data. These factors include: the long shelf life of FFP; significant delays from incident to return of SHOT TRALI questionnaires; an increase in the total number of SHOT reports from 146 in 1996-1997 to 606 in 2005 and 531 in 2006; a new donor exclusion since April 2004 that defers donors transfused since 1980 and a change in the SHOT definition for TRALI in 2006 from the occurrence of symptoms within 24 hours to symptoms within 6 hours of transfusion. Finally, the assessment of the probability of TRALI in each case is a clinical judgement rather than an exact science.

Implicated components and donors

TRALI cases proven to involve donors with leucocyte antibodies that match patient antigens (relevant antibody) have been analysed by implicated component from 2003 to 2006. Results are shown in figure 12. Cases involving FFP with proven relevant antibody have dropped from 10 in 2003 to none in 2005 or 2006. Cases involving platelets with a relevant antibody dropped from 8 in 2003 to 3 in 2005 and 1 in 2006. All cases with proven relevant antibody have involved female donors.

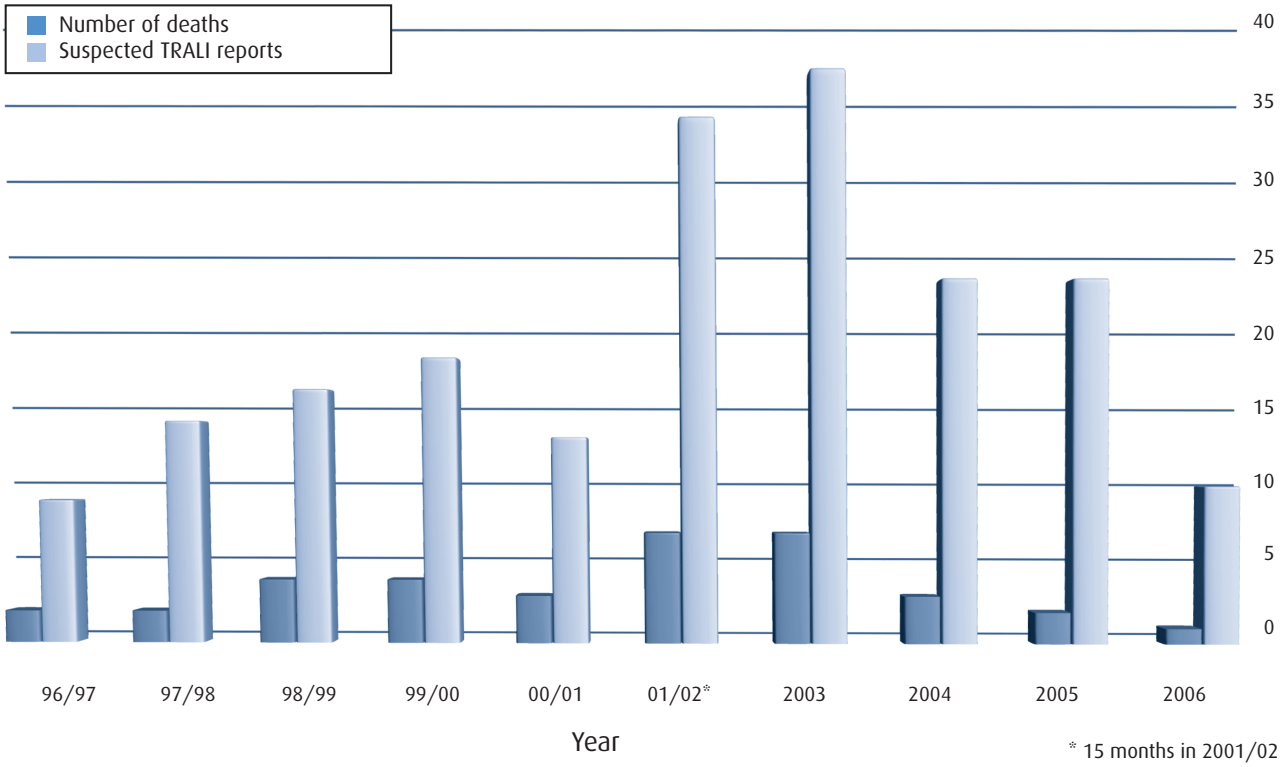
Figure 12
Cases of TRALI with relevant donor antibody analysed by implicated component and by year 2003-2006



Annual reports and deaths 1996-2006

Figure 13 shows the annual numbers of reports of suspected TRALI and the numbers of reported deaths at least possibly due to TRALI, each year from 1996. Annual reports of TRALI and deaths due to TRALI have both decreased since preferential male plasma policies were introduced.

Figure 13
Deaths at least possibly due to TRALI and number of suspected TRALI reports by year



American–European (A-E) Consensus definition compared with SHOT definition 2006 cases

Results are tabulated below; the resulting TRALI probability assessment is similar or the same in each case.

Table 32

Incident number	Other ALI risk	Circulatory overload/ cardiac failure	A-E Consensus definition category	SHOT TRALI category
2006-001-025-HV1-693	No	No	TRALI	Highly likely
2006/002/021/ HV1/876	Yes Haemorrhagic shock	No	Possible TRALI	Possible
2006-002-027-HV1-902	Yes Haemorrhagic shock	No	Possible TRALI	Possible
2006-003-007-HV1-004	No	No	TRALI	Highly likely
2006/003/017/ HV1/001	No	Yes	Not TRALI	Possible
2006/003/031/ HV1/005	No	Yes	Not TRALI	Unlikely
2006/004/027/ HV1/001	Yes Sepsis	No	Possible TRALI	Possible
2006/006/014/HV1-002	No	Yes	Not TRALI	Unlikely
2006/007/005/ HV1/009	No	No	TRALI	Probable
2006/007/018/ HV1/004	Yes Sepsis	Yes	Not TRALI	Unlikely

Case 1

A 64-year-old man had Waldenstrom's macroglobulinaemia. He was admitted for elective plasma exchange to treat hyperviscosity. The exchange was with albumin/saline replacement and was uneventful. Several hours later he was transfused with 2 units of FFP and 5 units of cryoprecipitate to correct abnormal clotting before removal of his femoral line. The plan was to discharge him after the line had been removed.

The patient developed chest pain (which is uncommon in TRALI cases), hypotension and severe hypoxia during transfusion of FFP and following 5 units of cryoprecipitate and 1 other unit of FFP. He was treated with oxygen, IV fluid, frusemide and steroids but continued to deteriorate and had a respiratory arrest. An anaesthetist intubated the patient, chest compression was applied to 'exude fluid.' and he was transferred to ITU. On arrival on ITU his oxygen saturation was 77%. There was then a gradual drop in BP and finally loss of cardiac output approximately two hours after his respiratory arrest. He died after failing to respond to cardio-pulmonary resuscitation.

Two of the cryoprecipitate donors had relevant antibodies including both HLA Class I and HLA Class II antibodies that matched three of the patient's HLA antigens: HLA-B42, HLA-DR4 and HLA-DR53. The case was assessed as highly likely to be due to TRALI and the reporter indicated that the death was probably due to TRALI (imputability 2).

Case 2

An 83-year-old man with myelodysplasia was transfused with platelets as a day case and developed shivers and mild dyspnoea after 10 mL of the first unit. He was given hydrocortisone and piriton and his symptoms seemed to settle, so transfusion of 2 units of apheresis platelets, both from the same donor, was completed. He went home but within one hour developed very marked shortness of breath and returned to hospital. He was cyanosed and tachycardic but not hypotensive; on auscultation he had a few scattered crackles. Oxygen saturation was 82% on air and rose to 95% on oxygen by facemask. He was admitted overnight, CRP was raised at 64 and he also had a raised Troponin T. He was treated with antibiotics for suspected infection and reviewed by cardiologist who felt he had sustained a non-ST elevation myocardial infarct (MI). His ECHO showed good LV function. CXR reported as: heart size upper limit of normal, both lower zones and right mid-zone deterioration compared with CXR at 3 days pre-transfusion. The consultant haematologist felt that the primary event was a respiratory reaction to transfusion and this was then complicated by an MI. Both of the intensivists on the national expert panel agreed that TRALI was possible and that investigation was warranted. The patient made a full respiratory recovery by the next day but was recorded by the reporter as having long-term morbidity because he had sustained an MI.

The platelet donor was female and had a history of 2 pregnancies in 1996 and 2002. She was found to have multiple HLA Class I and HLA Class II antibodies. The HLA Class II cognate antigen DR4 was present in the patient. The case was assessed as probably due to TRALI.

COMMENTARY

- TRALI remains a serious complication of transfusion with 3 probable or highly likely cases this year, 2 with serious consequences.
- One death was likely to have been related to TRALI; this is the lowest reported mortality since 1996.
- TRALI cases assessed as highly likely/probable have decreased from 22 in 2003 to 13 in 2004, 6 in 2005 and 3 in 2006.
- The TRALI case definition changed this year to exclude cases occurring more than six hours after transfusion. This is to be consistent with the recommendations of the American–European Consensus[32]. This change in definition was not introduced earlier by SHOT to allow a clearer assessment of the impact of the introduction of preferential use of male donor plasma for FFP and platelet pools.
- The smallest number of cases of suspected TRALI has been reported this year since 1996. At least two changes took place: the changed TRALI definition and the change to electronic reporting to MHRA and SHOT. The changed definition is unlikely to explain the reduction, because all suspected TRALI reports in 2004 and 2005 for which time of event was reported (43 of 46) occurred within 6 hours of transfusion. Electronic reporting may have inhibited some reporting. It is also possible that an incorrect assumption that all FFP is from male donors might have inhibited reporting in some cases.

- Sustained reductions in the number of TRALI reports, deaths and cases firmly implicating FFP and platelets in recent years most likely relate to the preferential use of male plasma for FFP and plasma for platelet pooling since late 2003 and the exclusion, since April 2004, of donors transfused since 1980.
- All cases were correctly referred to local BTS and patient samples were sent to the Reference Laboratory promptly. In only 1 case was it not possible to assess if a donor antibody matched a patient because of sample unavailability.
- Two reported cases were not investigated following advice from the National Expert Panel.
- Female donors were implicated in all cases in which a relevant leucocyte antibody was found (3 cases, 4 donors). Two cases involved antibodies with HLA specificities and 1 case with HNA antibodies. The implicated components were cryoprecipitate (2), platelets (1) and red cells in optimal additive solution (1).
- The number of cases of TRALI due to transfusion of platelets with a relevant donor antibody decreased from 8 in 2003 to 3 in 2004, 3 in 2005 and 1 in 2006.
- No case of TRALI owing to transfusion of FFP from a donor with a relevant donor leucocyte antibody was found this year or last year. This contrasts with 8 such cases reported in 2003 and 6 in 2004, all from female FFP donors.
- One case with proven relevant donor antibody concerned transfusion of red cells in optimal additive solution. This has been seen previously and indicates that less than 30mL of plasma can trigger TRALI. Another case concerned cryoprecipitate, a relatively low plasma component containing about 35mL plasma in single units, but in this case 2 cryoprecipitate donors had relevant antibodies including a combination of HLA Class I and HLA Class II antibodies that matched 3 of the patient's HLA antigens.
- NBS introduced preferential recruitment of male apheresis platelet donors in 2006 but existing female platelet donors continue to donate (approximately 25% donations). An NBS assessment of screening female apheresis donors for leucocyte antibodies is planned and trials have taken place of replacement of 70% plasma in platelets with platelet additive solution. The Welsh Blood Service already routinely screen all female apheresis donors for HLA antibodies.
- FFP from the WBS, NIBTS and SNBTS is 100% male, and plasma for platelet pooling from WBS and SNBTS is also 100% male. NBS in 2006 produced 86% of FFP and 86% of plasma for platelet pooling from male donors.

RECOMMENDATIONS

- UK Blood Services must work towards and maintain 100% male FFP, and male plasma for platelet pools.

  Action: UK Blood Services

- UK Blood Services should continue to investigate and apply methods to reduce the continuing risk of TRALI associated with apheresis donations, reducing the number of female donors on the panel, and testing those remaining for HLA antibodies.

  Action: UK Blood Services

Carried over from 2005:

- Hospital staff should continue to be aware of TRALI and report possible cases to the local BTS to facilitate investigation. Detailed clinical information is needed to allow accurate clinical assessment of these cases. Blood samples (clotted and EDTA) from affected patients should be sent for laboratory investigation early. Continued education of all relevant staff about this condition is encouraged.

  Action: HTTs

- Cases should be evaluated early by the consultant(s) involved and prompt discussion with the BTS is helpful. A team approach is recommended, with expertise included from the haematologist and chest physician and/or ITU consultant.

  Action: Clinical users of blood and Consultant haematologists with responsibility for transfusion

10. Post-Transfusion Purpura

Definition:

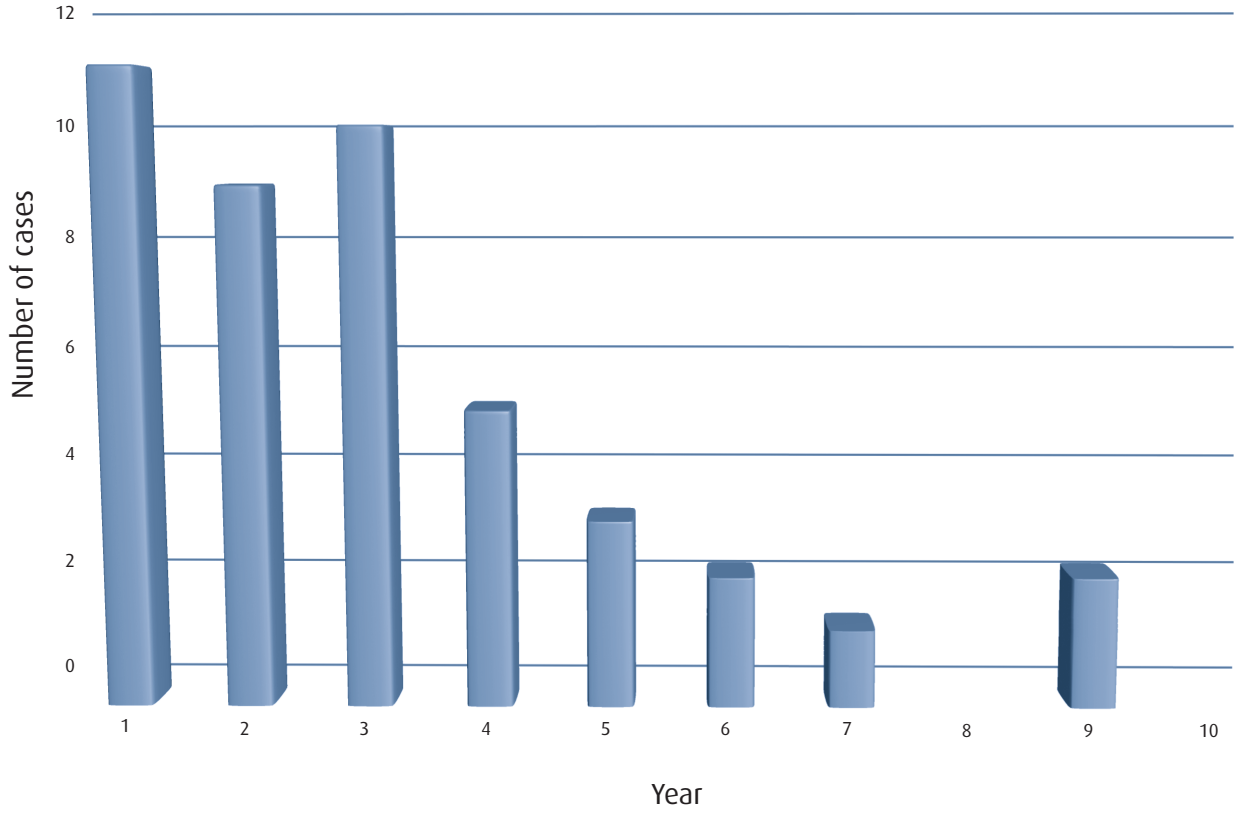
Post-transfusion purpura was defined as thrombocytopenia arising 5-12 days following the transfusion of red cells associated with the presence in the patient of antibodies directed against the HPA (Human Platelet Antigen) systems.

Only 1 case was reported as possible PTP but this case was subsequently withdrawn by the reporters who had evidence that transfusion was not the cause of the patent's thrombocytopenia.

COMMENTARY

- No confirmed case of PTP was reported this year. The graph (Figure 14) shows the number of cases of confirmed PTP reported to SHOT each year since 1996. The drop in the number of cases of PTP since the introduction of universal leucodepletion in 1999 has been maintained.

Figure 14
Number of cases of confirmed PTP reported to SHOT each year



- As reported last year, there has also been a change in the transfusion profile preceding the development of PTP since the introduction of leucodepletion. Before April 2000 all 29 patients, for whom components were recorded, had received red cell transfusion without platelet transfusion before PTP developed. After April 2000, 5 of 8 patients with PTP had received both RBC and platelet transfusion and only 3 had received RBC alone.

RECOMMENDATIONS

- Clinicians need to maintain awareness and a high index of suspicion of this rare but treatable complication of transfusion.
- When PTP is suspected there should be referral to a platelet reference laboratory for relevant investigation.

11. Transfusion-Associated Graft-versus-Host Disease

Definition (updated 2005)

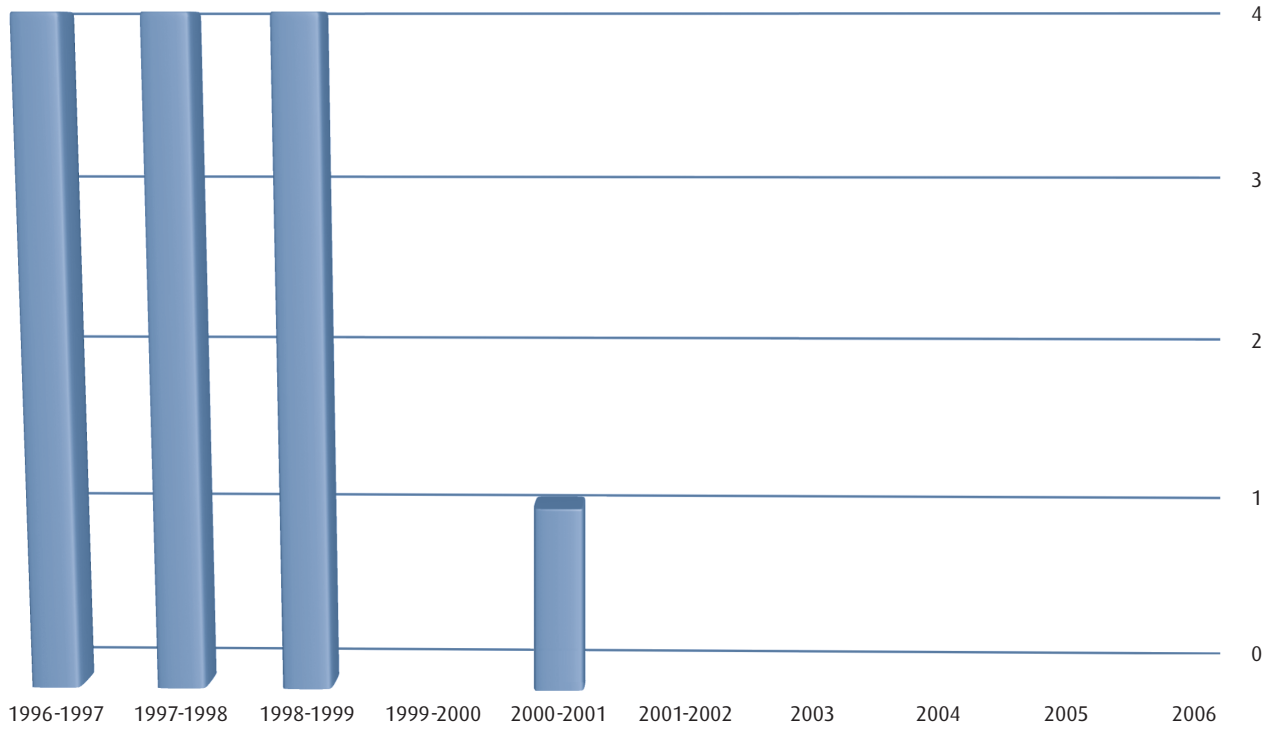
Transfusion-associated graft-versus-host disease is a generally fatal immunological complication of transfusion practice, involving the engraftment and clonal expansion of viable donor lymphocytes, contained in blood components in a susceptible host. TA-GVHD is characterised by fever, rash, liver dysfunction, diarrhoea, pancytopenia and bone marrow hypoplasia occurring less than 30 days following transfusion. The diagnosis is usually supported by skin/bone marrow biopsy appearance and/or the identification of donor-derived cells, chromosomes or DNA in the patient's blood and/or affected tissues.

There were no new cases of TA-GVHD during the 2006 reporting period.

COMMENTARY

The last case of TA-GVHD to be reported to SHOT was in the reporting period 2000-2001 in a patient with acute B-lymphocytic leukaemia (B-ALL). The following graph shows the number of cases of TA-GVHD reported to SHOT each year since the scheme began in 1996.

Figure 15
Number of cases of TA-GVHD reported to SHOT each year



- Leucodepletion of all blood components was introduced by the UK Blood Services in 1999 and this is the most likely reason for the marked reduction in the number of reports of this condition. The single case report in 2000-2001 demonstrates, however, that a risk remains.
- Gamma irradiation of blood components is currently the only accepted method to prevent TA–GVHD in susceptible individuals[33].
- TA-GVHD has a very high mortality; death was reported in all 13 cases reported to SHOT in the past.
- Eighty-two patients who had a requirement to receive irradiated blood (in accordance with BCSH guidelines) but who did not receive it are identified in the IBCT Chapter. Fortunately, none developed the condition.

RECOMMENDATIONS

- Gamma or X-ray irradiation to 25 Gy of blood components for those at risk of GVHD remains essential. BCSH Blood Transfusion Task Force Guidelines define groups requiring this prophylaxis[34].
- New chemo or immuno-therapeutic regimens must be evaluated for their potential to predispose individuals to TA-GVHD. New guidelines are in preparation from the BCSH.
- Awareness of groups at risk of this condition and knowledge of the risk factors, symptoms and signs must be maintained by all involved in the transfusion process.
- Good communication is required in all cases but particularly when patient care is shared between different hospitals. Hospitals must have clear protocols to ensure accurate information relating to this risk is communicated in a timely manner. Utilisation of a patient card and leaflet are recommended: an example is the BCSH/NBS leaflet available from NBS Hospital Liaison or via the NBS hospitals website.

12. Transfusion-Transmitted Infections

Definition

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion and no evidence of an alternative source of infection;

  and, either

- at least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

  or

- at least one component received by the infected recipient was shown to contain the agent of infection.

Reports of suspected transfusion-transmitted infections

During 2006, 28 reports of suspected transfusion-transmitted infections were made from blood centres throughout the UK to the NBS/HPA Centre for Infections Surveillance. All UK blood centres contributed to the scheme. One additional report was also received from a hospital to MHRA (via SABRE) that had not been reported through routine blood service surveillance (see commentary below); this case has been included in the numbers below (29 cases in total).

Two reports (bacteria) were determined to be TTIs according to the above definition. Twenty-five cases were concluded as not transfusion-transmitted infections (5 hepatitis B [HBV], 2 hepatitis C [HCV], 1 hepatitis A [HAV], 1 HIV, 2 CMV and 14 bacteria). One (hepatitis C) involved a multi-transfused patient (dates of transfusion between 1997 and 2005) that could neither be confirmed nor refuted as a TTI, as 3 donors could not be traced. One case (HBV) is pending complete investigation.

A further report was received from the Health Protection Agency of a clinical diagnosis of vCJD in a blood transfusion recipient.

Case report of transfusion-transmitted Klebsiella pneumoniae

One recipient (54-year-old male) with AML received 1 unit of pooled platelets (3 days old). Within 5 minutes of starting the transfusion he became acutely unwell and the transfusion was terminated. The patient was given hydrocortisone and piriton, but died 24 hours post transfusion. The findings confirmed death due to overwhelming septic shock subsequent to either live Gram negative bacteraemia, or as a result of a lethal exposure to Gram negative bacterial endotoxin. *Klebsiella pneumoniae* was isolated from the platelet pack, but not from a sample taken from the patient at the time of transfusion. The platelet pack had been screened as part of a field trial of the BacT/ALERT* system prior to issue and was negative after 24 hours' culture. Four associated red cell units and 3 associated FFP units were investigated and were negative. Skin and throat swabs were taken from all 4 donors and were also negative. Archived plasma donations from all donors were investigated by PCR for *Klebsiella*-specific DNA but none was detected. Extensive investigation of the blood centres at which the component was manufactured, tested and issued did not reveal the presence of *Klebsiella* spp. on or in any of the equipment involved. The investigation concluded that this was bacterial contamination of a pooled platelet unit with *Klebsiella pneumoniae*; no source of the contamination was found.

* BacT/ALERT is a fully automated blood culture system for detecting bacteraemia and fungaemia based on detection of CO_2 production by any organisms present. As well as its clinical application in the diagnosis of bacteraemia, it is validated 'CE marked' and FDA approved for quality control testing of apheresis and platelet concentrates [35,36].

Case report of transfusion-transmitted Streptococcus bovis

A 90-year-old female recipient was found to have low platelet count and bleeding symptoms during an outpatient visit and received pack two of a three part apheresis platelet donation (3 days old). One hour later the patient collapsed on her journey home. She was admitted to A&E where she was resuscitated. On readmission to hospital she was febrile, tachycardic, hypotensive and hypoxic. Cultures were taken and broad spectrum antibiotics and fluids were started. In the initial 48 hours after transfusion she developed signs of mild cardiac failure and renal impairment. *Streptococcus bovis* (biotype II) was cultured from the patient's blood cultures and from the apheresis platelet pack. Pulsed field gel electrophoresis (PFGE) on the isolates from the patient's blood and platelet pack revealed them to be indistinguishable. The patient made a full recovery.

Because of the strong association between *S. bovis* bacteraemia and gut pathology, the donor was referred to the local hospital for colonoscopy and ongoing management. This revealed diverticular disease, together with two small dysplastic tubular villous adenomas, which were removed. It is suspected the donor's diverticular disease was the cause of the *S. bovis* contamination of the platelet donation. The donor was removed from the donor panel and thanked for many previous platelet donations.

Pack 1 of the apheresis donation was transfused to another patient, also on day 3 of the shelf-life, with no adverse reaction. The recipient's blood cultures were negative and the remnants of the implicated pack were investigated but no organisms were isolated. Pack 3 had also been transfused successfully on day 3 of the platelet shelf-life, but the empty pack was not available for investigation. This recipient was on high-dose antibiotics at the time of the transfusion.

This case was concluded to be a proven case of bacterial contamination of an apheresis platelet unit with *Streptococcus bovis*, the source of which was asymptomatic bacteraemia in a donor with undiagnosed asymptomatic diverticular disease.

Reports of further incidents

vCJD

In early 2007, the Health Protection Agency gave notification of a fourth case of vCJD infection associated with blood transfusion. In late 1997, a recipient received transfusion of a number of blood components. The donor of one of the units of non-leucodepleted red cells developed symptoms of vCJD about 17 months after this donation. The recipient developed symptoms of vCJD 8.5 years after receiving the transfusion. The donor is the same as that of Case 3, reported in the SHOT 2005 report. The recipient has since died.

(For more information on variant CJD see http://www.cjd.ed.ac.uk.)

Reports from previous years

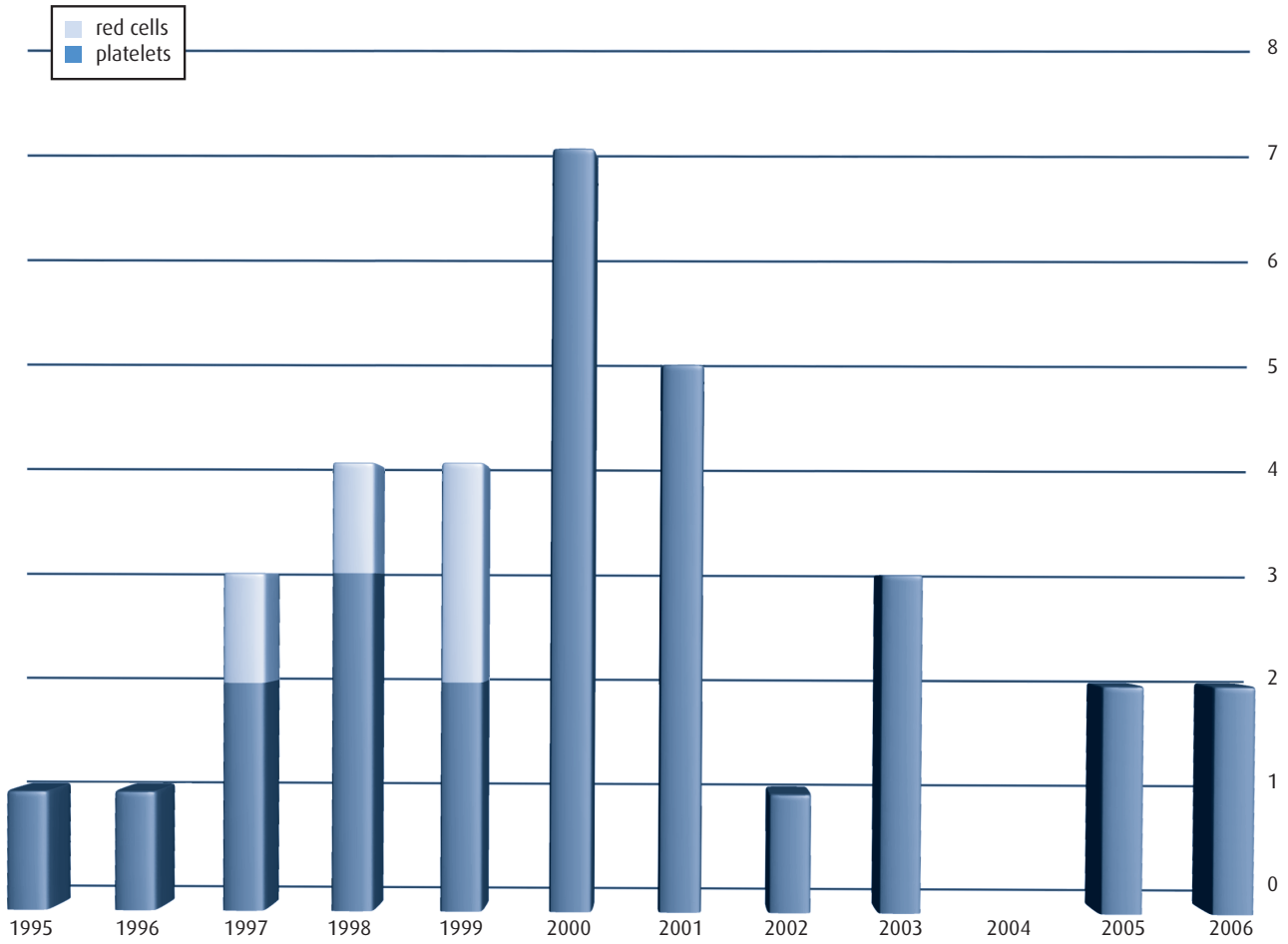
The case reported as pending in 2004 (HHV-8) is now nearing completion; all donors have been recalled and have provided blood samples for HHV-8 testing. Results will be reported when available. The pending HCV case from the 2005 report has been confirmed as not transfusion-transmitted.

Cumulative bacterial data

Since 1995, 33 cases of transfusion-transmitted bacterial infection have been reported (figure 16), of which 9 recipients died (8 due to the transfusion and 1 due to their underlying disease). The majority of these cases (n=29) relate to platelet units (10 apheresis and 19 pooled). In 2004 there was a further incident involving contamination of a pooled platelet pack with *Staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely (not included in figure 16).

Further cumulative data[37] are available at http://www.hpa.org.uk/infections/topics_az/BIBD/menu.htm.

Figure 16
Confirmed bacterial transfusion-transmitted infections, by year of transfusion and type of unit transfused (Scotland included from 10/1998)



COMMENTARY

- The number of cases reported to the scheme is small and fluctuations are to be expected. Infectious complications following transfusion differ from non-infectious complications in several ways that may affect their identification and investigation. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of incidents in a particular year can therefore accrue over subsequent years, and the number ascertained by the end of any period may not necessarily represent the number of infections transmitted. The reporting of incidents involving acute infections that tend to be clinically apparent and diagnosed within days after receipt of the infectious transfusion, such as bacteraemia, may be relatively complete, but incidents involving chronic viral infections may not. This year there were no confirmed viral transmissions, which is consistent with the current very low estimated risk of HIV, HCV, HBV and HTLV infectious donations entering the UK blood supply. The estimated risk in the UK is broadly similar to that in other northern European countries and lower than southern European countries[37].

For current UK risks see http://www.hpa.org.uk/infections/topics_az/BIBD/est_freq_uk.htm).

- One case was initially reported via MHRA as transfusion-transmitted bacteria, which had not been reported via routine NBS/HPA surveillance. This case had been notified to the local blood centre by the HTT and the pack was reported to have been sent to the blood centre. However, it was not received by the blood centre and was therefore not tested. Upon further investigation, the case was determined to be not caused by transfusion, as the isolate identified in the patients blood culture was different to that identified in the pack by the hospital microbiology laboratory. Hospital transfusion teams should ensure that all samples sent for bacterial investigation to their hospital laboratory should record that the sample is part of an investigation into a suspected bacterial transfusion transmission and that all results are collated by the hospital team, prior to making the confirmatory report to MHRA. Additionally, correct sampling of the pack is important to avoid external contamination or the introduction of environmental contaminants. Advice can be obtained from the blood services. Guidance for hospitals can be found

on the NBS hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer.

- The report of a fourth case of vCJD infection increases the concern about the risk of vCJD transmission by blood transfusion. The patient is one of a small group of recipients of blood from donors who later developed vCJD. These recipients have been notified of their possible exposure to vCJD and are under surveillance: this represents active case finding. All 4 cases to date relate to the transfusion of blood components prior to the introduction of leucodepletion; none relate to plasma products. Since 1997 the blood services have introduced a number of precautionary measures against the risk of vCJD. This includes leucodepletion of all blood components (since 1999), the use of methylene blue virally inactivated FFP obtained outside the UK for children under 16, importation of plasma for fractionation, imported solvent detergent (SD) treated FFP for adult patients with thrombotic thrombocytopenic purpura (TTP) and the exclusion of donors who have received a blood transfusion in the UK since 1980.
- The Standing Advisory Committees (SAC) of the Joint UKBTS/NIBSC Executive Liaison Committee (JPAC) make recommendations to the Guidelines for the Blood Transfusion Services in UK in relation to the prevention of transfusion-transmitted infections. For example, SAC Transfusion-Transmitted Infection (SACTTI) regularly reviews the residual risk of transfusion-transmitted HCV, HIV, HBV and HTLV infections to assess any need for additional testing methods, such as HIV RNA testing, HBV DNA or anti-HBc. SAC Care and Selection of Donors ensures donor deferral criteria are optimal in terms of exclusion of donors with behaviour that may put them at increased risk of contracting transfusion transmissible infections. Major decisions are considered by the DH Microbiological Safety of Blood, Tissues and Organs committee.

RECOMMENDATIONS

- Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately, both to MHRA and the blood services. Guidance for hospitals can be found on the NBS hospitals website: http://www.blood.co.uk/hospitals/library/request_forms/aer. Other services need to be discussed with the supply blood centre.

  Action: HTTs

- Despite good donor selection guidelines, some donors with infections might go on to donate, as in the donor above with undiagnosed diverticular disease. This is rare. Surveillance of testing blood donors for viral infections shows that a tiny proportion of donors have viral infections[38]. It is important for UK Blood Service collection teams to remain vigilant for signs or symptoms of disease and risk factors for infection in potential donors and ensure that guidelines are adhered to, in order to reduce the risk of transmission of blood-borne infections.

  Action: UK Transfusion services

- Hospitals should consult the blood services about the investigation of transfusion reactions suspected to be due to bacteria. Attention should be paid to the sampling and storage of implicated units or their residues and packs returned to blood services for testing. The case reported via MHRA that did not reach the blood service highlighted the need for laboratory reports within each hospital to be clearly marked as part of a suspected transfusion reaction and copied to the HTT. (See above weblink or http://www.transfusionguidelines.org.uk/index.asp?Publication=REGS&Section=23&pageid=789 for more information.)

  Action: HTTs

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14. Glossary of Terms

ACSBTO	Advisory Committee on Safety of Blood Tissues and Organs
AHG	Antihuman globulin
AHTR	Acute haemolytic transfusion reaction
ALG	Antilymphocyte globulin
ALI	Acute lung injury
ALL	Acute lymphoblastic leukaemia
AML	Acute myeloblastic leukaemia
ARDS	Acute respiratory distress syndrome
ATD	Adult therapeutic dose
ATR	Acute transfusion reaction
BBTS	British Blood Transfusion Society
BCC	Blood Consultative Committee
BCSH	British Committee for Standards in Haematology
BMS	Biomedical scientist
BP	Blood pressure
BSQR	Blood safety and quality regulations
BTS	Blood Transfusion Service
CA	Competent Authority
CABG	Coronary artery bypass graft
CEO	Chief executive officer
CMO	Chief medical officer
CMV	Cytomegalovirus
CNST	Clinical negligence scheme for trusts
CRP	C-reactive protein
CVP	Central venous pressure
CXR	Chest X-ray
DAT	Direct antiglobulin test
DHTR	Delayed haemolytic transfusion reaction
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid
DTR	Delayed transfusion reaction
ECG	Electrocardiogram
ECHO	Echocardiogram
EDTA	Ethylenediaminetetraacetic acid
EPR	Electronic patient record
ESR	Erythrocyte sedimentation rate
EUD	European Union directive
FBC	Full blood count
FFP	Fresh frozen plasma
GI	Gastrointestinal
GP	General Practitioner
HAV	Hepatitis A virus
HBc	Hepatitis B core
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HHV-8	Human herpes virus-8
HIV	Human immunodeficiency virus
HLA	Human leucocyte antigen
HNA	Human neutrophil antigen
HPA	Human platelet antigen or Health Protection Agency
HTC	Hospital transfusion committee
HTLV	Human T-cell leukaemia virus
HTT	Hospital transfusion team
IAT	Indirect antiglobulin test
IBCT	Incorrect blood component transfused
IBGRL	International blood group reference laboratory
IBMS	Institute of Biomedical Science
Ig	Immunoglobulin
INR	International normalised ratio
ITU	Intensive therapy unit
IV (i.v.)	Intravenous
JPAC	Joint professional advisory committee
LDH	Lactate dehydrogenase
MB	Methylene blue
MCT	Mast cell tryptase
MDS	Myelodysplastic syndrome
MHRA	Medicines and Healthcare products Regulatory Agency
MI	Myocardial infarct
MLA	Medical laboratory assistant
MSBTO	Microbiological safety of blood tissues and organs
NBS	National Blood Service
NBTC	National Blood Transfusion Committee (England)
NHL	Non Hodgkins Lymphoma
NHSLA	NHS litigation authority
NHS QIS	NHS Quality Improvement Scotland
NIBSC	National Institute for Biological Standards and Control
NIBTS	Northern Ireland Blood Transfusion Service
NICE	National Institute for Clinical Excellence
NPSA	National Patient Safety Agency
OA	Optimal additive
O&G	Obstetrics and gynaecology
PC-Aph	Apheresis platelets
PC-BC	Buffy coat-derived platelets
PCR	Polymerase chain reaction
PFGE	Pulsed-field gel electrophoresis
PICU	Paediatric intensive care unit
PLTaph	Apheresis platelets
PMETB	Postgraduate Medical Education & Training Board
PTP	Post-transfusion purpura
RAADP	Routine antenatal anti-D prophylaxis
RBRP	Right blood to right patient
RNA	Ribonucleic acid
SABRE	Serious adverse blood reactions and events
SAC	Standing Advisory Committee
SACTTI	Standing Advisory Committee on transfusion-transmitted infection
SAE	Serious adverse event
SAR	Serious adverse reaction
SCID	Severe combined immunodeficiency disease
SD	Solvent detergent
SHO	Senior house officer
SNBTS	Scottish National Blood Transfusion Service
SOB	Shortness of breath
SOP	Standard operating procedure
TACO	Transfusion-associated circulatory overload
TA-GVHD	Transfusion-associated Graft-versus-host disease
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
TTP	Thrombotic thrombocytopenic purpura
UKBTS	UK Blood Transfusion Services
vCJD	Variant Creutzfeldt Jakob disease
WBS	Welsh Blood Service

15. Acknowledgements

The Steering Group would like to take this opportunity to thank the following individuals and organisations for their contributions without which the publication of this tenth SHOT Annual Report would not have been possible:

- All hospitals who have participated in SHOT reporting
- The Blood Transfusion Services of the United Kingdom for funding and support
- The Royal College of Pathologists for their support and use of facilities
- Kirk Beard – NBS, for the provision of data relating to the issue of blood components from the Transfusion Services of the UK
- Judith Chapman – Blood Stocks Management Scheme, for the provision of data relating to the issue of blood components to hospitals in the UK
- Neil Soni, Imperial College Medical School and Cliff Morgan, Royal Brompton Hospital for expert review of the TRALI cases
- Clinical and Scientific staff in hospitals and reference laboratories who have contributed to the clinical and laboratory investigation of cases
- Paul Ashford and Ceri Frampton – WBS, for maintenance of the SHOT website
- MHRA and Assad Afzal of Charles McKenzie Consulting for provision of the SABRE system and ongoing technical support
- Angela Allen, Personal Assistant to Dorothy Stainsby
- Tahera Lakha, Personal Assistant to Clare Taylor
- Christine Smith, Personal Assistant to Hannah Cohen
- David Gifford, for expert input into the design and production of the report, and Frances Grant, copy-editor

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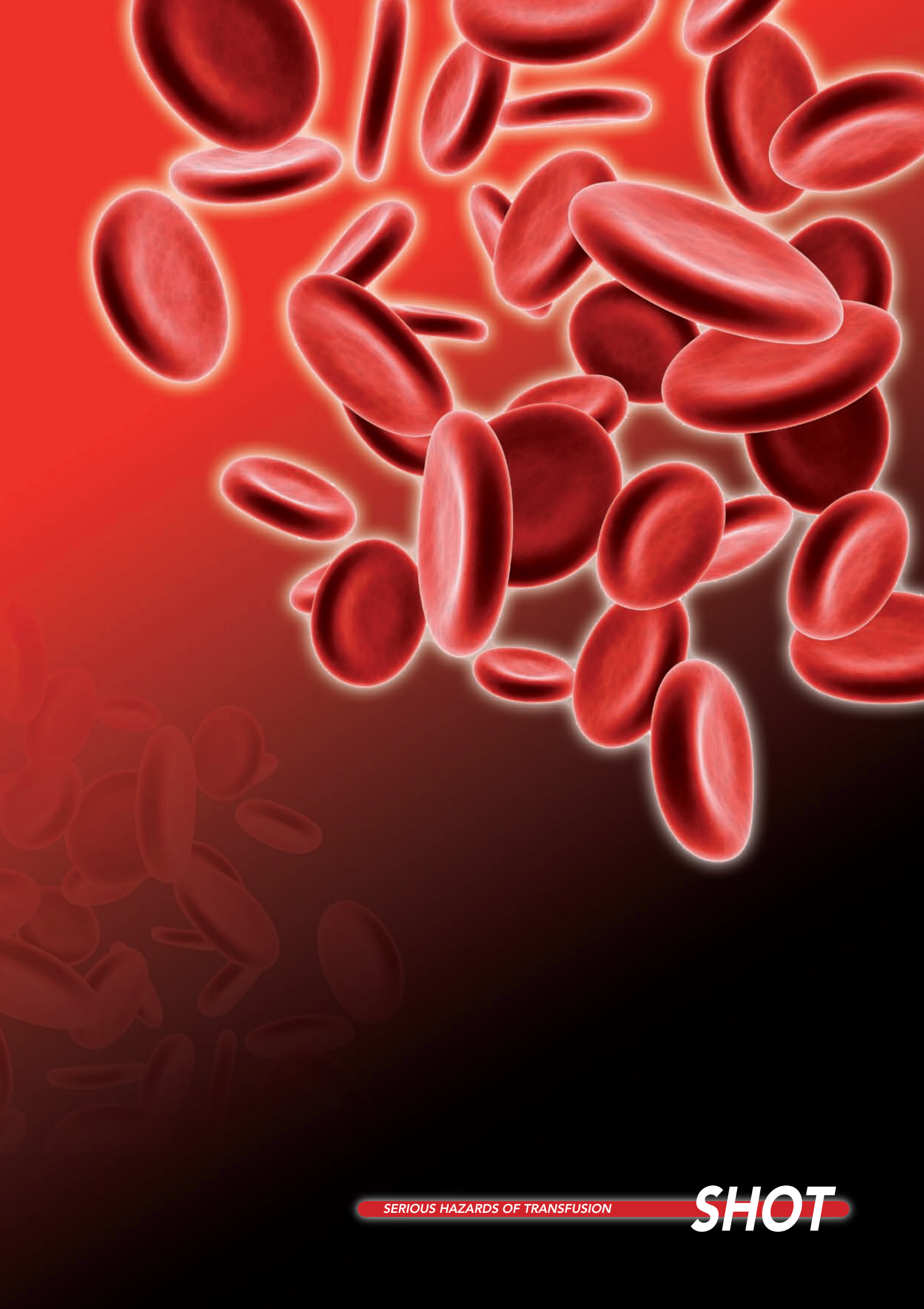

SERIOUS HAZARDS OF TRANSFUSION

SHOT