

SERIOUS HAZARDS OF TRANSFUSION

ANNUAL REPORT

2003

Affiliated to the Royal College of Pathologists

British Blood Transfusion Society, British Society for Haematology

Faculty of Public Health Medicine, Institute of Biomedical Science

Institute of Healthcare Management, NHS Confederation

Health Protection Agency Communicable Disease Surveillance Centre

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Royal College of Obstetricians and Gynaecologists

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by The Serious Hazards of Transfusion Steering Group

National co-ordinators:	Dr Dorothy Stainsby Ms Katy Davison (Health Protection agency CDSC)
Scheme Manager:	Mrs Hilary Jones (SHOT office)
Data Collection Specialist:	Mrs Aysha Boncinelli (SHOT Office)

Writing Group

Stainsby D	Cohen H
Jones H	Knowles S
Milkins C	Chapman C
Gibson B	Davison K
Norfolk D R	Taylor C
Revill J	Asher D
Atterbury CLJ	Gray A

on behalf of the SHOT Steering Group

Requests for further information should be addressed to:

Non-infectious hazards

SHOT Office
Manchester Blood Centre
Plymouth Grove
Manchester
M13 9LL

Tel: 0161 251 4208
Fax: 0161 251 4395
Email: hilary.jones@nbs.nhs.uk
dorothy.stainsby@nbs.nhs.uk

Website: <http://www.shot-uk.org>

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Infectious hazards

Ms. Katy Davison
Clinical Scientist
Health Protection agency CDSC
61 Colindale Avenue
London NW9 5EQ

Tel: 020 8200 6868
Fax: 020 8200 7868
Email: katy.davison@hpa.org.uk

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Glossary of Terms

ALI	Acute Lung Injury
ALT	Alanine Aminotransferase
ARDS	Acute respiratory distress syndrome
ATR	Acute transfusion reaction
BBTS	British Blood Transfusion Society
BCSH	British Committee for Standards in Haematology
BMS	Biomedical scientist
CABG	Coronary artery bypass graft
CAT	Column agglutination technology
CDSC	Communicable Disease Surveillance Centre
CEO	Chief Executive Officer
CMO	Chief Medical Officer
CMV	Cytomegalovirus
CNST	Clinical Negligence Scheme for Trusts
CVS	Chorionic villus sampling
CXR	Chest X-Ray
DAT	Direct antiglobulin test
DHTR	Delayed haemolytic transfusion reaction
DNA	Deoxyribonucleic acid
DOH	Department of Health
DTR	Delayed transfusion reaction
EC	European Commission
ECMO	Extracorporeal membrane oxygenation
EU	European Union
FFP	Fresh frozen plasma
HAV	Hepatitis A virus
HBc	Hepatitis B core
HBs Ag	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDN	Haemolytic disease of the newborn
HDU	High Dependency Unit
HIV	Human immunodeficiency virus
HLA	Human leucocyte antigen
HNA	Human neutrophil antigen
HPA	Human platelet antigen
HPA CDSC	Health Protection Agency Communicable Disease Surveillance Centre
HTC	Hospital Transfusion Committee
HTLV	Human T-cell leukaemia virus
HTT	Hospital Transfusion Team
IAT	Indirect antiglobulin test

Glossary of Terms

IBCT	Incorrect blood component transfused
ICU	Intensive care unit
INR	International normalised ratio
Ig	Immunoglobulin
IUT	Intrauterine transfusion
LISS	Low ionic-strength saline
MB	Methylene blue
MHRA	Medicines and Healthcare Products Regulatory Authority
MSBT	Microbiological Safety of Blood and Tissues for Transplantation
NBS	National Blood Service
NBS/HPA	National Blood Service/Health Protection Agency
NBTC	National Blood Transfusion Committee (England)
NEQAS	National External Quality Assurance Scheme
NISS	Normal ionic-strength saline
NPSA	National Patient Safety Agency
PCR	Polymerase chain reaction
PCT	Primary Care Trust
PTI	Post-transfusion infection
PTP	Post-transfusion purpura
PTR	Post-transfusion reaction
RNA	Ribonucleic acid
RTC	Regional Transfusion Committee
SHA	Strategic Health Authority
SHO	Senior House Officer
SPOT	Specialist practitioners of transfusion
TA-GVHD	Transfusion-associated graft-versus-host disease
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
TTP	Thrombotic thrombocytopenia purpura
vCJD	Variant Creutzfeldt-Jakob disease
VSD	Ventricular septal defect

1 Keynote Message

CHANGE AND EVOLUTION IN HEALTHCARE DEMAND GREATER HAEMOVIGILANCE

With this 7th annual report, SHOT provides an increasingly authoritative analysis of serious transfusion hazards in the UK and an evidence base for blood safety initiatives, policies and guidelines. This report is condensed to make it more user-friendly with detailed data available on the SHOT website www.shot-uk.org. Recommendations are targeted at specific groups or bodies to maximise their effectiveness.

Current figures re-emphasise the importance of errors in the transfusion process. In 2003, 358 reports were received of incorrect or inappropriate blood component transfused (IBCT), a further increase of 25% over the previous 12 months. Errors continue to occur at all stages of the transfusion process; misidentification of patients, blood samples and blood components being the main source of errors. It is likely that the increased number of reports is related to the establishment, as recommended in 'Better Blood Transfusion' HSC 2002/009,¹ of hospital transfusion teams (HTTs) and Specialist Practitioners of Transfusion (SPOTs), who drive greater vigilance, and hence reporting of errors which may have previously gone unrecognized.

Eighty-five per cent of hospitals reported that they participated in SHOT in 2003. However, only 47% reported adverse events, possibly reflecting a lack of HTTs and SPOTs in these Trusts. Individual hospitals can make a positive contribution to transfusion safety by active participation in SHOT, so that the picture of transfusion risks is as complete and accurate as possible. Thorough and systematic investigation of all adverse events is essential, requiring clinical input from the consultant haematologist with responsibility for blood transfusion, who should sign off each case report. Evidence of active participation is likely to be required in the future as part of external reviews of clinical governance arrangements, e.g. by the Health Care Commission.

On a more encouraging note, despite the increased number of errors reported, there is an overall downward trend in the number of ABO incompatible transfusions (Figure 3). This suggests that we may be starting to see the improvement in the proportion of 'serious' events compared to overall events, which characterises a developing safety culture. Tools for analysis of errors have been developed by the National Patient Safety Agency (NPSA)² who have rolled out a programme of training and support. **Examples of how such tools can be effective in establishing the root cause of incidents can be found on the SHOT website.**

Clinical audit is a useful tool with which to monitor the implementation of policies and processes. The recent National Comparative Audit of Transfusion,³ carried out jointly by the National Blood Service (NBS) and the Royal College of Physicians, identified variation and poor practice in the administration of blood. In 2001, the Scottish National Blood Transfusion Service, in collaboration with NHS hospitals in Scotland, undertook a 3-year study of a transfusion-practitioner-led clinical effectiveness programme, including audit and education. Observable improvements in transfusion practices were demonstrated at the intervention sites. A motivated and enthusiastic transfusion practitioner, supported by a local transfusion team, was able to raise awareness of blood transfusion throughout the hospital.⁴ Audit and feedback at local level can also be effective in improving practice and, together with education and training, is a key role of the SPOT. HTTs and SPOTs must now be established in all trusts. The Chief Medical Officer's (CMO's) National Blood Transfusion Committee (NBTC) in England and its counterparts in Scotland, Wales and Northern Ireland were constituted with a remit to promote implementation of Better Blood Transfusion. SHOT looks to these bodies to take a proactive lead role in driving forward blood safety issues in hospitals.

Eight of the 34 articles of the new European Union (EU) Directive on Blood Transfusion⁵ are directly applicable to hospital blood banks; this becomes UK law in February 2005 and mandates notification of adverse events/reactions. The Directive requires positive traceability of all blood components from donor to patient, placing great demands on the quality and integration of hospital IT systems. The UK Government must designate a competent authority to regulate Blood Establishments by February 2005, and must also indicate how it will demonstrate compliance by hospital blood banks and for haemovigilance. A national guideline on the specification and performance of blood bank computer systems, developed by the British Committee for Standards in Haematology (BCSH), will be welcome.

Safety in the hospital transfusion laboratory is compromised by difficulties in recruitment and retention of suitably qualified staff and increasing demands on them as a result of moves towards 24/7 hospital activity. Recruitment to new roles, such as doctors' assistants, may attract experienced biomedical scientists (BMS) away from the bench. The initiatives outlined in 'Making the Change'⁶ which include the development of National Occupational Standards for Healthcare Scientists, flexible career pathways, improved status through higher specialist training and a stronger regulatory framework through the Health Professions Council, provide a much needed opportunity to increase and consolidate the workforce and must be implemented.

We are pleased that the IT Working Group of the CMO's NBTC in England has put the needs of the transfusion community firmly on the agenda of bodies, such as the Design Authority, responsible for setting standards and priorities in the NHS IT strategy. The current SHOT annual report again highlights that failures of communication of special requirements or lack of availability of previous transfusion history contribute to 'wrong blood' events. It is crucial that NHS IT systems have the ability to use unique patient-specific identifiers, such as the NHS Number, so that essential information is available to all who need it. Systems for positive patient ID have considerable potential to improve patient safety in blood transfusion as well as other areas such as drug administration. The development of integrated systems across disciplines will have important economic as well as patient-safety benefits. SHOT encourages these initiatives and emphasises the need for standards and establishing minimum specifications across the NHS. SHOT data will be an important source of information for the evaluation of IT solutions.

During the past 12 months, important blood safety initiatives have been introduced by the blood services. Precautions to reduce the incidence of bacterial contamination of platelets are being implemented and in England fresh frozen plasma (FFP) is now made almost exclusively from male donors in order to reduce the risk of transfusion related acute lung injury (TRALI). Other blood services await the impact of the latter precaution with great interest, but it should be remembered that increasing awareness of this condition and hence increased reporting may mask a reduction in incidence. Once again, SHOT data will be of importance in the evaluation of the impact of these new blood safety measures.

This year's report includes the first documented case of possible transfusion transmitted variant Creutzfeld-Jakob Disease (vCJD). It is highly unlikely that this case would have been identified without the transfusion epidemiology surveillance scheme undertaken jointly by the blood services and the vCJD Surveillance Unit.⁷ In the UK, precautions in place to reduce the risk of prion transmission, include leucodepletion of all blood components, the use of viral-inactivated FFP obtained outside the UK for children born after 1 January 1996, importation of plasma for fractionation and the exclusion of donors who have received a blood transfusion in the UK after 1980. This latter precaution, implemented in April 2004, is expected to result in a 3–5% reduction in availability of donated blood. There is therefore an increased imperative towards blood conservation, requiring a co-ordinated approach led at national level to maximise effectiveness. It is crucial that there is also a parallel initiative to monitor for adverse effects of alternatives to transfusion, which will necessitate appropriate co-ordination between SHOT, Medicines and Healthcare Products Regulatory Authority (MHRA) and other experts in the field.

Since its first report, SHOT has recommended the establishment of an overarching body to evaluate and prioritise blood safety initiatives. It is hoped that the forthcoming review of the Department of Health Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation will extend its remit and membership, and empower it to take on this role.

As always, we would like to thank hospital staff who participate in SHOT and ensure its continuing success.



Dr Hannah Cohen MD FRCP FRCPath

Chair, SHOT Steering Group



Dr Dorothy Stainsby FRCP FRCPath

SHOT National Medical Co-ordinator.

2 Main Findings and Recommendations

SUMMARY OF MAIN FINDINGS

Participation

In 2003, 351/415 (85%) hospitals returned cards stating that they participated in the SHOT scheme. This is an 8% drop compared with 2001-2002, due to the fact that the SHOT office has lacked manpower resource to pursue non-responders and cannot do so in future. Evidence of participation is required for the Clinical Negligence Scheme for Trusts (CNST) and may be required for other accreditation schemes. Reporting of adverse reactions to blood transfusion will become mandatory with implementation of the EU Directive.⁵ It is the responsibility of hospitals to ensure that they return the card in good time in order to obtain the required receipt.

Hospital transfusion teams should note that:

- Participation cards will be mailed in January/February each year. They should contact the SHOT office if they have not received the card by mid-February.
- The card should be completed and returned as soon as possible and strictly by the deadline.
- They should receive a receipt within 4 weeks and should contact the SHOT office if not.
- The SHOT office retains records of reports and next year will contact hospitals if there is a discrepancy between our records and the number of reports stated on the return.

195/415 hospitals stated that they reported incidents; the level of active participation is therefore unchanged at 47%. A total of 480 initial reports were received in 2003, and 449 questionnaires analysed plus 8 TTI reports not on standard SHOT questionnaires.

Incorrect blood component transfused ("wrong blood") incidents

In 2003, 358 reports were received; a 25% increase over the previous equivalent 12 month period and 75% of all reports received this year. It is likely that the establishment in hospitals of transfusion teams and SPOTS is resulting in greater vigilance and hence reporting of previously unrecognised errors. Although the total number of errors reported continues to increase, there is an overall downward trend in the number of ABO incompatible transfusions reported, suggesting that we may be starting to see the improvement in the proportion of 'serious' events compared to overall events which characterises a developing safety culture.

Again this year multiple errors have contributed to 'wrong blood' events with a total of 588 errors occurring in 348 analysed cases and multiple errors in 52%.

The distribution of errors in IBCT cases is remarkably consistent, with approximately 70% of errors occurring in clinical areas (30% prescription, sampling, request and 40% collection and administration) and 30% in laboratories. Again this year the commonest error (156/588) was failure of the pre-transfusion bedside checking procedure.

A detailed breakdown of types of error can be found on the SHOT website.

Outcomes of errors this year were 33 ABO incompatible transfusions, of which 4 were also RhD incompatible (26 incompatible red cell transfusions and 7 incidents of incompatible FFP, cryoprecipitate or platelets). There were 22 cases of unintended RhD incompatible transfusions and 22 cases where other red cell antigen incompatible transfusions were given. There was one possible transfusion related death but no definite or probable cases. Sixteen patients suffered major morbidity.

"Near-miss" events

906 near miss reports were received this year from 163 hospitals

The picture of "near miss" reporting is consistent, showing sample errors to be by far the most numerous (50% in 2000/2001, 59% in 2001/2002 and 60% in 2003). Common sources of error were;

- Patient mis-identification.
- Spurious haematology results due to dilute samples from "drip arms" and samples in syringes dispensed into tubes without mixing.
- Point-of-care (POC) testing variations.
- Labelling of samples remote from the patient and pre-labelling of specimen tubes.

- Addressograph labels used wrongly or placed in wrong patients' notes.

Anecdotal evidence from reporting hospitals suggests that "near miss" events are frequent but under-reported and discussions are underway concerning how better to collect this data in the future.

Immune complications

Thirty-six case reports of suspected TRALI were analysed in 2003. Nine patients died; 1 death was considered to be definitely due to transfusion, 7 possibly due to transfusion and 1 unrelated. Twenty-two patients suffered short term major morbidity and five minor morbidity.

Plasma rich components were implicated in 20 of 21 cases with proven leucocyte incompatibility between donor and patient.

There were 39 analysable reports of acute transfusion reactions (ATR) accounting for 1 probable transfusion related death and 2 cases of major morbidity.

Twenty-five delayed haemolytic transfusion reactions (DHTR) were analysed, a marked reduction from last year's 47 reports. It is unlikely that the incidence of these reactions has fallen, and there is a concern DHTRs are under-recognised.

Again this year there were no reports of transfusion-associated graft-versus-host disease (TA-GVHD), and only 1 report meeting the SHOT definition of post-transfusion purpura (PTP).

Transfusion-transmitted infections

In 2003, 38 reports of possible transfusion-transmitted infections (TTIs) were made to the surveillance scheme. After the investigation had been completed, eight reports were classified as probable TTIs (2 Hepatitis B virus (HBV), 1 Human Immunodeficiency virus (HIV), 1 Hepatitis A virus (HAV), 1 malaria and 3 bacterial contaminations). One of the cases of bacterial contamination died. Twenty-four reports were found not to be related to transfusion and 3 had an undetermined source. Full investigations on 2 cases are still pending. The UK's National CJD Surveillance Unit and the NBS reported the first possible case of transfusion transmitted vCJD, identified in 2003 following the death of a transfusion recipient.⁷

SHOT in patients under 18 years of age

59 case reports in 2003 (13%) involved patients less than 18 years of age, 53 of which were reports of IBCT.

Twenty-eight of 348 (8%) of analysed IBCT incidents occurred in patients less than 12 months of age. The percentage of red cells transfused to this group has been reported to be 1.2%⁸ suggesting a disproportionately high incidence of transfusion errors in this age group (see chapter 4 IBCT). 20/28 of these (71%) involved infants in their first month of life, reflecting the pattern of transfusion in the paediatric population.

It is clear from some of the reported errors that there is lack of awareness amongst laboratory, nursing and medical staff of the special needs of paediatric recipients of blood and blood components.

Nine paediatric patients suffered morbidity or potential morbidity but recovered including 5 who developed intra-vascular haemolysis and 2 RhD negative females who received RhD positive red cells.

Autologous transfusion

SHOT has received no reports this year of adverse reactions relating to autologous pre-deposit donation. There have been three reports of adverse events relating to the re-infusion of autologous blood, two of these are included in the IBCT chapter and one was an ATR following re-infusion of salvaged red cells.

With increasing emphasis on blood conservation techniques it is important that adverse events are reported and documented, so that the relative risks of alternatives to allogeneic blood transfusion can be assessed.

GENERAL RECOMMENDATIONS

1. Participation in SHOT must be active

In every hospital, every serious transfusion adverse event must be identified, fully investigated and reported to SHOT. Thorough and systematic investigation of all errors, immunological reactions and post-transfusion infections, with appropriate involvement of the local blood centre, is essential, and requires clinical input from the consultant haematologist with responsibility for blood transfusion, who should sign off each case report.

Action: Trust Chief Executive Officers (CEOs) through Hospital Transfusion Committees (HTCs) and risk management structures, consultant haematologists, hospital staff involved in the blood transfusion process

2. An open learning and improvement culture must continue to be developed in which SHOT reporting is a key element

Development of a culture in which there is an appreciation of the potential for error and an emphasis on learning from adverse events is key to participation in SHOT. Fear of criticism or disciplinary action and uncertainty about the consequences of reporting blood transfusion errors leads to underreporting. This results in lost opportunities to learn from errors and improve practice.

The evolution of a more open approach to reporting has other potential implications for SHOT reporters; for example, it would in future be possible for SHOT to provide comparative data to regional transfusion committees and user groups who request it. SHOT will continue to protect the confidentiality of individuals and hospitals, nevertheless there may be benefits to be gained by a more open approach, particularly when bidding for resources or evaluating the efficacy of various intervention strategies.

Action: Trust CEOs through risk management structures, staff involved in the blood transfusion process

3. Resources must be made available in Trusts to ensure that appropriate and effective remedial action is taken following transfusion errors

Action: Strategic Health Authorities (SHAs), Primary Care Trusts (PCTs), Trust CEOs through HTCs and risk management structures

4. Hospital transfusion teams must be established and supported

As recommended in HSC 2002/009,¹ hospitals involved in blood transfusion must establish and support a HTT to drive greater vigilance, and hence reporting of errors which may have previously gone unrecognised. The HTT requires clinical leadership ideally from a consultant haematologist, with dedicated sessions, supported by a SPOT (nurse, BMS or medical professional) and the blood bank manager. Adequate administrative resources must be made available.

Action: Trust CEOs through HTCs

5. Hospital blood bank laboratory staffing must be sufficient for safe transfusion practice

Hospitals must ensure that blood transfusion laboratories have adequate numbers of appropriately trained BMSs to cover the 24-hour working day, including a core of permanent blood transfusion laboratory staff. National standards should be established for manpower appropriate to the level of workload and this should be subject to inspection.

The initiatives outlined in 'Making the Change',⁶ which include the development of National Occupational Standards for Healthcare Scientists, flexible career pathways, improved status through higher specialist training and a stronger regulatory framework through the Health Professions Council, provide an opportunity to increase and consolidate the workforce and must be implemented.

Action: Trust CEOs, clinical directors of pathology, professional and accrediting bodies

6. Education and training is of key importance for safe and effective blood transfusion practice

i) Blood transfusion must be included in the curriculum for student nurses, and medical undergraduates. This teaching must include all aspects of blood transfusion safety and should not be confined to basic blood group serology.

Action: Deans of Schools of Nursing and Medical Schools

ii) Blood transfusion should also be included in the curriculum of specialist trainees, particularly anaesthetists and critical care nurses who are usually at the 'front line' of transfusion of vulnerable patients, e.g. unconscious patients

in theatres and intensive care units (ICUs) and patients requiring massive blood transfusion.

Action: Medical Royal Colleges, Universities

iii) The disproportionate number of errors in paediatric patients reflects lack of knowledge by clinical and laboratory staff of their transfusion requirements. A BCSH guideline on blood transfusion in neonates and older children which details special requirements for these patients has recently been published⁹ and should be implemented.

Action: Staff in paediatric units and transfusion laboratories

iv) An ongoing programme of education and training in blood transfusion is essential for hospital staff, including consultants and BMSs, involved in the transfusion process. A web based 'tool kit' for education and training in blood transfusion developed in Scotland is available.¹⁰ Implementation of the administration tool throughout the UK will require additional resource.

Action: Local, regional and national transfusion committee network

v) This year there were several instances in which inappropriate remedial action was taken following errors, both within the laboratory and clinical areas. The regional transfusion committee structure, facilitated by the blood services, 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. An important role of the Regional Transfusion Committee (RTC) is to support translation of guidelines into local practice.

Action: RTCs and user groups

7. Mechanisms must be put in place for appropriate and timely communication of information regarding special transfusion requirements

Poor communication is an important cause of adverse events. In the longer term, IT offers robust solutions, but interim arrangements are required and must be locally implemented and audited.

Action: Trust CEOs through HTC, HTTs

8. Appropriate use of blood components must be strenuously promoted and alternatives to transfusion evaluated. The latter must include monitoring for serious adverse effects.

Appropriate use of blood is an integral part of any blood safety strategy and should be monitored by regular audit. Guidance on the use of blood components is available on www.transfusionguidelines.org.uk and as the Handbook of Transfusion Medicine¹¹, and is revised in accordance with current BCSH guidelines. Attention is drawn to the recent BCSH guidelines on the use of FFP, cryoprecipitate and cryosupernatant.¹² Continued efforts are needed to ensure that practitioners and patients have ready access to up-to-date, simple, consistent and user-friendly information on best practice.

As a consequence of the first documented case of probable transfusion transmitted vCJD, included in this year's report there is an increased imperative towards appropriate use of blood together with a nationally led and appropriately resourced evaluation of alternatives to allogeneic blood transfusion. It is crucial that there is a parallel initiative on monitoring for serious adverse effects of alternatives to transfusion so that the relative risks of pharmacological alternatives to blood and autologous transfusion are compared with those of allogeneic transfusion.

Action: Department of Health (DOH), CMO's NBTC, Trust CEOs through HTCs, clinicians administering blood transfusion, hospital transfusion teams

9. Electronic aids to transfusion safety should be assessed and developed at national level

As noted in previous SHOT Reports, we believe that information technology has great potential to improve transfusion safety.

i) Blood transfusion must be included on the agenda of the Design Authority and other bodies responsible for setting standards and priorities in the NHS IT strategy

During the last 12 months the IT Working Group of the CMO's NBTC in England has succeeded in getting the needs of the transfusion community firmly on the agenda of those bodies, such as the Design Authority, responsible for setting standards and priorities in the NHS IT strategy. It is crucial that NHS IT systems have the ability to use unique patient-specific identifiers, such as the NHS Number, so that blood banks can share information (eg the presence of alloantibodies or the need for irradiated or cytomegalovirus (CMV) negative blood products) between hospitals.

ii) National standards and specifications should be developed for blood bank laboratory computer systems

There is a clear need to develop national standards and specifications for blood bank laboratory computer systems to ensure the range of functions, flexibility and connectivity essential for safe modern practice. Blood banks are moving rapidly into areas such as electronic selection of compatible blood, automated testing and computer-controlled issue from blood refrigerators, all of which demand absolutely secure patient/specimen ID, information transfer and decision algorithms. The new EU Directive on Blood Transfusion,⁵ with its requirement for the traceability of all blood products from donor to patient, also places great demands on the quality and integration of hospital IT systems. The BCSH guidelines on blood bank computer systems are under review and detailed guidance on the specification and performance of blood bank computer systems will be welcome.

iii) Bar-code technology for positive patient identification, and to control and monitor access to hospital blood refrigerators, should undergo continued development and evaluation co-ordinated at national level

At the clinical interface, there are now at least two effective and well-validated commercial electronic systems based on bar-code technology available to control and monitor access to hospital blood refrigerators. Extension of electronic control to the bedside (sampling and blood administration) continues to be the subject of field studies as the technology becomes more reliable and user friendly. As noted in previous SHOT Reports, we believe that these systems for positive patient ID have considerable potential to improve safety of blood transfusion as well as in areas such as drug administration. The development of integrated systems across disciplines will have important economic as well as patient-safety benefits to hospitals. SHOT encourages these initiatives and, once again, emphasises the need for setting standards and minimum specifications across the NHS.

Action: CMO's NBTC, Design Authority, British Blood Transfusion Society (BBTS), BCSH, NPSA, enthusiasts in the field

10. The CMO's NBTC in England and its counterparts in Scotland, Wales and Northern Ireland should take a proactive lead in driving forward blood safety issues in hospitals

These bodies were constituted with a remit to promote implementation of Better Blood Transfusion. SHOT looks to these bodies to take a proactive lead role in driving forward blood safety issues in hospitals.

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

11. There is a need for a national body, with relevant expertise and resource, to advise government on priorities for improvements in transfusion safety

Each SHOT report contains specific recommendations. However SHOT has no authority over implementation and cannot monitor compliance. Decision-making pathways are needed to enable data from SHOT to influence blood safety policy and prioritisation of resource allocation for the development, evaluation and implementation of improvements in transfusion safety.

Action: DOH

SPECIFIC RECOMMENDATIONS

Incorrect Blood Component Transfused

- Hospital risk management committees must ensure that all staff undertaking venepuncture for blood sampling must have received the necessary training and have their practical competency formally assessed and recorded. Blood samples should be taken from a free flowing venepuncture site, and the tube should be filled to capacity and inverted gently several times to adequately mix the sample and any anticoagulant. The person taking the sample must complete the tube label before leaving the patient, checking the details are correct with the patient and against the ID wristband or equivalent.

Action: Hospital risk management committees

- Hospital risk management procedures should include 'drills' for high risk situations such as massive transfusion, involving all relevant staff.

Action: Hospital risk management committees

- Prevention of TA-GVHD in patients receiving purine analogues is the responsibility of prescribers, but can and must be supported by the pharmaceutical industry and pharmacists and by suppliers of laboratory IT systems. All patients should

receive an information card and leaflet and haematologists must ensure that there is an effective system of flagging special transfusion requirements in the laboratory. Referrals for shared care must include timely communication of all relevant information.

Action: Clinicians prescribing purine analogues and administering blood transfusion; hospital transfusion teams; pharmacists, pharmaceutical industry; suppliers of laboratory IT systems

- Hospital blood bank laboratory staffing must be sufficient for safe transfusion practice. Hospitals must ensure that blood transfusion laboratories have adequate numbers of appropriately trained biomedical scientists to cover the 24-hour working day, including a core of permanent blood transfusion laboratory staff. Standards should be established for manpower appropriate to the level of workload and this should be subject to inspection.

Action: Clinical directors of pathology, professional and accrediting bodies

- Paediatric units undertaking transfusion must ensure that staff are educated in the special transfusion requirements of children. Laboratory IT systems should be regularly updated to support implementation of new guidelines.

Action: Paediatricians and laboratory staff responsible for transfusion of paediatric patients; HTCs

- The most important contribution which could now be made to the safety of blood transfusion would be an initiative to improve the safety of the bedside pretransfusion checking procedure. This will require investment in education and audit, and also in evaluation and implementation of suitable information technology. The CMO's NBTC has the necessary remit to take this forward.

Action: CMOs NBTC through regional and hospital transfusion committees: hospital transfusion teams

Immunological reactions

Acute transfusion reactions

- The guideline dealing with the investigation and management of acute transfusion reactions is awaited and emphasis should be placed upon the need for identifying underlying causes that will impact upon the choice of future component therapy.

Action: BCSH

- There is continued evidence of inappropriate clinical use of FFP, despite the availability of recently published BCSH guidelines on appropriate use¹² and existing recommendations for the management of warfarin reversal.¹³ Further local audits and educational programmes should be encouraged through the Transfusion Committee network.

Action: Regional and hospital transfusion committees

- The recent BCSH transfusion guideline for neonates and older children⁹ states that group A recipients should receive group A platelets, but accepts that group O can be transfused as a second alternative provided that these components are lacking high titre anti-A or anti-B. However Transfusion Service testing for high titre anti-A/B cannot confidently exclude all dangerous donations and the Services should be encouraged to ensure that sufficient group A platelets are always available for these patients.

Action: UK Transfusion Services

Delayed transfusion reactions

- Investigation of a suspected DHTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. This may involve referral to a reference centre.

Action: Hospital transfusion laboratories

- Automated systems or changes to indirect antiglobulin test (IAT) technology should be validated using a range of weak antibodies to ensure appropriate sensitivity.

Action: Hospital transfusion laboratories

- Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies. 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: Hospital transfusion laboratories supported by UK Transfusion Services

- 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: BCSH and BBTS

Post-transfusion purpura

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

Transfusion-related acute lung injury

- Every effort must be made to avoid unnecessary transfusion of plasma rich blood components including FFP and platelets.

Action: Clinicians administering blood transfusion

- FFP continues to be associated with risks of reactions including TRALI and should only be used when clinically indicated in accordance with BCSH guidelines¹². Guidelines for the management of high international normalised ratios (INRs) due to warfarin therapy should also be followed.¹³

Action: Clinicians administering blood transfusion

- Transfusion of whole blood should be discouraged.

Action: HTTs

- Hospital staff should continue to be aware of TRALI and report possible cases to the local Blood Centre to facilitate investigation. Continued education of all relevant staff about this condition is encouraged.

Action: HTTs, clinicians administering blood transfusion

- Cases should be evaluated early by the consultant(s) involved and there should be early liaison with the local Blood Centre. A team approach including the haematologist and chest physician and/or ICU consultant will definitely be helpful.

Action: Clinicians administering blood transfusion, chest physicians and ICU consultants

- Serological investigation of suspected TRALI cases must include tests for antibodies to human leucocyte antigen (HLA) Class II, HLA Class I and granulocyte specific antigens.

Action: Reference laboratories

- The NBS TRALI risk reduction project has led to the implementation of procedural changes such as using plasma from male donors only for FFP. UK Transfusion Services should continue with implementation of such initiatives; attention is also being paid to the plasma contribution to platelet pools and reducing the risk of TRALI posed by female apheresis donors.

Action: UK Transfusion Services

Transfusion-associated graft-versus-host disease

- Gamma irradiation of blood components for those at risk of GVHD remains essential. BCSH Blood Transfusion Task Force Guidelines define groups requiring this prophylaxis.
- Awareness of the potential for this condition 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. Provision of the BCSH/NBS patient card and leaflet are also recommended.
- New chemo or immuno-therapeutic regimens must be evaluated for their potential to predispose individuals to TA-GVHD. Regular update of guidelines is required to include up to date recommendations relating to drugs and protocols with potent immunosuppressive effects.

Action: Clinicians prescribing purine analogues and administering blood transfusion, HTTs, pharmacists, pharmaceutical industry, suppliers of laboratory IT systems

Transfusion-transmitted infections

- Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components. These include:
 - Continuation of diversion of the first 20-30 mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site)
 - Careful attention to adequate cleansing of donors' arms
 - Adherence to BCSH guidelines (1999)¹⁴ with regard to the visual inspection of blood components for any irregular appearance immediately prior to transfusion.
- UK Blood Services should continue to review and implement options available to minimise the risk of bacterial contamination of platelets.
- Hospitals should consult guidelines and the blood service about the investigation of transfusion reactions suspected to be due to bacteria. Attention should be paid to the sampling and storage of implicated units.
- Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately.

Patients less than 18 years of age

- Laboratory, nursing and medical staff should all be aware of the special consideration of component selection and/or requirement for product manipulation for neonatal and paediatric transfusion. Specific education of these staff in paediatric transfusion practice is crucial.

Action: HTTs

- The wearing and checking of wrist or ankle namebands is essential in the paediatric age group, who may not be able to identify themselves verbally, and may be the last opportunity to identify an error arising earlier in the transfusion chain.

Action: Staff of paediatric units

- The recent BCSH transfusion guideline for neonates and older children⁹ states that group A recipients should receive group A platelets, but accepts that group O can be transfused as a second alternative provided that these components are lacking high titre anti-A. However, Transfusion Service testing for high titre anti-A cannot confidently exclude all high titre anti A donors and they should be encouraged to ensure that Group A platelets are always available for these patients.

Action: UK Transfusion Services

- The importance of good and accurate communication at every level in transfusion practice must be emphasised to prevent unnecessary error.

Action: All involved in the transfusion process**Autologous transfusion**

- All adverse events associated with autologous donation and re-infusion should be reported to SHOT so that the relative risks of alternatives to allogeneic transfusion can be assessed.

Action: HTTs

3 Cumulative Data 1996 - 2003

This year, in keeping with the major chapters, most of the cumulative data is available on the SHOT website. The only figures presented here this year are the numbers of initial report forms and questionnaires received.

Initial report forms received: 2191 Questionnaires analysed: 2087

Figure 1

Initial reports by incident 1996/97 – 2003 (n=2191)

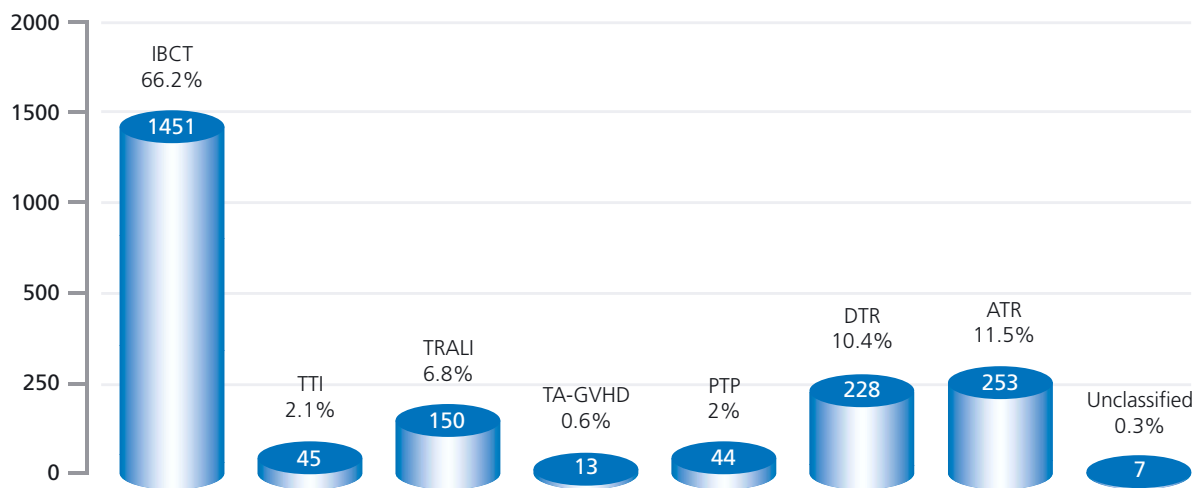
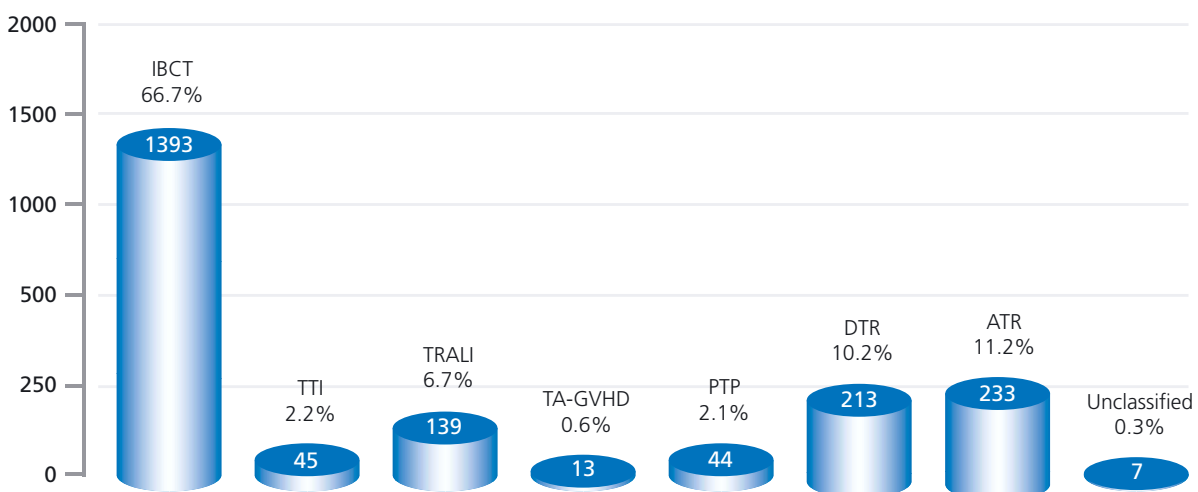


Figure 2

Questionnaires by incident 1996/97 – 2003 (n= 2087)



4 Incorrect Blood Component Transfused

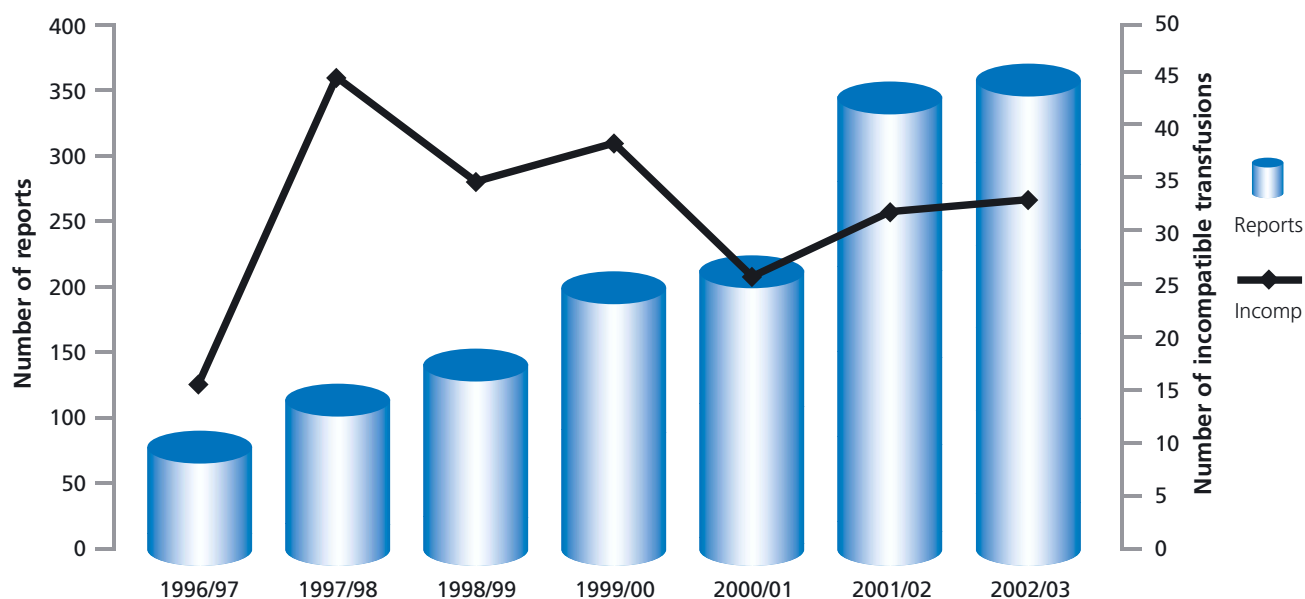
Definition

This section describes all reported episodes where a patient was transfused with a blood component or plasma product which did not meet the appropriate requirements or which was intended for another patient.

In the 12 month period Jan to Dec 2003, 358 new initial reports were received. This is a 25% increase over the previous equivalent 12 month period and IBCT reports comprised 75% of all reports received this year. It is likely that the establishment in hospitals of transfusion teams and SPOTS is resulting in greater vigilance and hence reporting of errors which may have previously gone unrecognised. Although the total number of adverse events reported continues to increase, there is an overall downward trend in the number of ABO incompatible transfusions reported (Fig 3), suggesting that we may be starting to see the improvement in the proportion of 'serious' events compared to overall events which characterises a developing safety culture.¹⁵

Figure 3

ABO incompatible transfusions since 1996



This chapter analyses 348 completed questionnaires, including 22 which were outstanding from the previous year. Completed questionnaires are outstanding on 32 initial reports and will be analysed next year. In addition, 61 reports were withdrawn as not meeting the criteria for IBCT and 1 has been "written off" due to failure to submit a completed questionnaire within an appropriate timescale.

All names in the vignettes are fictitious.

Analysis of reported errors

Analysis of the gender, age of recipients and blood components implicated in the incident can be found on the SHOT website.

The IBCT questionnaire requests much detail regarding the circumstances of events and adverse outcomes and this information is used to analyse each case individually and draw conclusions regarding the distribution and types of errors. Much of the raw data obtained from the questionnaires is available on the website. This chapter seeks to highlight and illustrate some of the important issues identified from reported incidents.

Errors occur in the transfusion of patients of all ages and in the administration of all types of components. It is notable that this year 28/348 (8%) of IBCT incidents related to patients under the age of 12 months. In a recent study on the epidemiology of blood transfusion⁸ the proportion of red cells transfused to this age group was 1.2%, so it would appear that there is a disproportionately high incidence of errors involving these patients. This finding is discussed in more detail in Chapter 12.

Outcomes

Of the 348 fully analysed cases there were 33 ABO incompatible transfusions of which 4 were also RhD incompatible, (26 incompatible red cell transfusions and 7 incidents in which patients received incompatible FFP, cryoprecipitate or platelets). In addition there were 22 cases of unintended RhD incompatible transfusions and 22 cases where other red cell antigen incompatible transfusions were given.

Mortality and morbidity

This year there were no definite or probable transfusion related deaths due to incorrect blood component transfused and only one possible case. The outcome of all IBCT cases is summarised in Table 1 below.

Major morbidity is defined as one or more of:

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

Table 1

Outcome of cases of incorrect blood component transfused (n=348)

Category	Survived / no ill effects	Major morbidity	Died unrelated to transfusion	Died possibly related to transfusion	Died probably related to transfusion	Died definitely related to transfusion	Outcome unknown	TOTAL
ABO incompatibility	19	8	5	1	0	0	0	33
RhD incompatible	18	4	0	0	0	0	0	22
ABO/RhD compatible	45	0	4	0	0	0	0	49
Other red cell incompatibility	20	1	1	0	0	0	0	22
Inappropriate transfusion	32	2	2	0	0	0	0	36
Special requirements not met	103	1	3	0	0	0	0	107
Anti-D	24	0	0	0	0	0	0	24
Other	54	0	1	0	0	0	0	55
Total	315	16	16	1	0	0	0	348

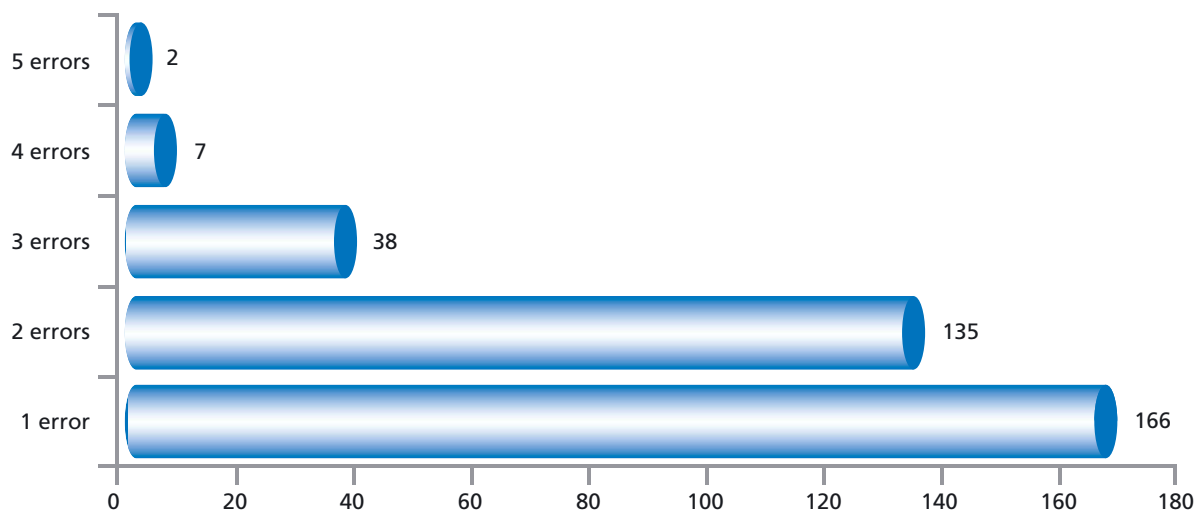
Multiple errors

Again this year multiple errors have in many cases contributed to 'wrong blood' events as shown in Fig 4. There were a total of 588 errors occurring in 348 analysed cases, with multiple errors in 52%. In some cases these have been separate but contributory errors, but in the majority a primary error has occurred which subsequent checks have failed to detect. The final opportunity to detect an earlier error is the bedside check, which, as last year, was the most common site of failure.

Events due to single errors are fewer than last year but are of particular concern, as these, such as patient misidentification at the sampling stage or transposition of samples in the laboratory, indicate critical stages in a process where errors cannot subsequently be detected. Review of systems is required if such errors are to be prevented in the future.

Figure 4

Multiple errors continue to contribute to many "wrong blood" transfusions

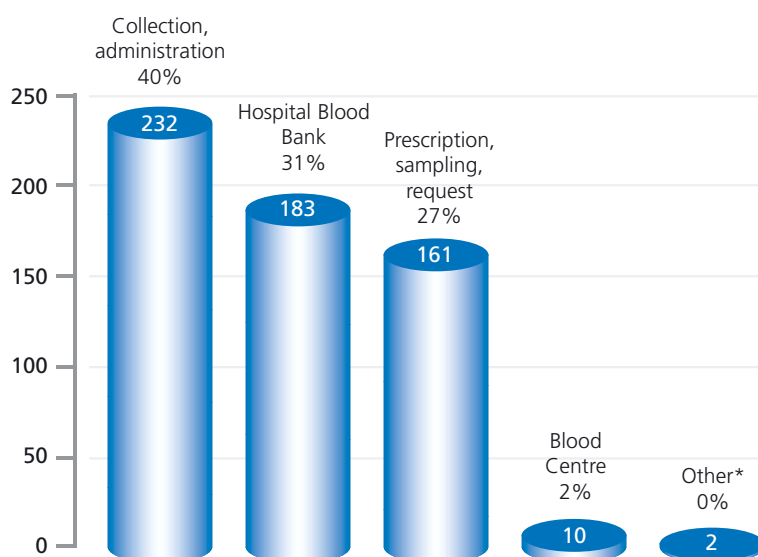


Distribution of errors

Figure 5 shows the distribution, according to the main reporting categories, of a total of 588 errors from the analysis of 348 completed reports. [A more detailed analysis of the distribution of total errors is available on the SHOT website.](#)

Figure 5

Distribution of total errors according to the main reporting categories



*Other = errors in software made by IT department

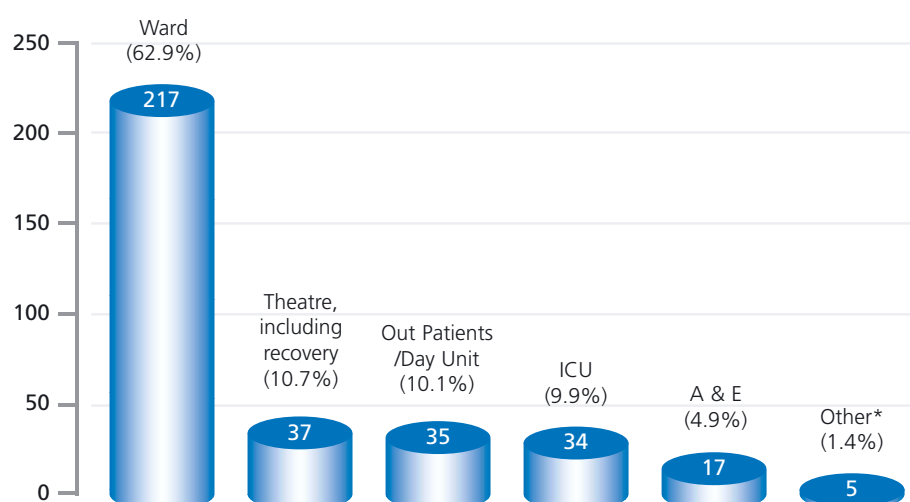
The distribution of errors in IBCT cases is remarkably similar to last year, with approximately 67% of errors occurring in clinical areas and 31% in laboratories. This year there has been a slight increase in the proportion of laboratory errors (28% last year) and a reduction in the proportion of collection and administration errors (43% last year). A detailed breakdown of types of error can be found on the SHOT website.

Site of transfusion

Three hundred and thirty-three reports gave information regarding the site of transfusion. In the absence of denominator data on blood transfusion activity, it can only be noted that clinical areas where there is a high ratio of nursing staff to patients are by no means exempt from errors. In all of these environments, factors likely to contribute to errors include inability of the patient to confirm their identity, identification wristband hidden or removed for venous access, and staff under stress because of clinical urgency.

Figure 6

Site of transfusion when error occurred in a clinical area



*Other = 3 x GP surgery, 1 x Community, 1 x Ambulance

Errors in prescription, requesting of blood components and patient sampling n=161

This year there were 161 errors in 154 cases at the prescription, request, and sampling stage. In 44% of cases the primary error occurred at this stage of the process. Approximately half of all errors at this stage (88/161) related to failure to indicate special transfusion requirements. This section also includes errors in blood sampling and labelling, potentially leading to ABO incompatible transfusion. SHOT analysis of 'near-misses' and clinical audit of samples rejected by laboratories¹⁶ have also highlighted the importance of errors at this stage.

Samples from wrong patient

On 10 reported occasions, the sample used for pre-transfusion testing had been taken from the wrong patient, and, because the patient had not been previously grouped, the error could not be detected. One of these errors was not detected until 6 months later when the laboratory received a further sample. Five patients received ABO incompatible blood as a result of sample errors, 4/5 suffered major morbidity; one patient (case 1) was already terminally ill and died 3 weeks later.

Case 1 Misguided teamwork leads to incompatible transfusion

A terminally ill patient was admitted as an emergency through A & E with a haemoglobin level of 74g/L. A nurse offered to take a sample for group and crossmatch, but took the sample from the wrong patient and handed it unlabelled to the Senior House Officer (SHO), who labelled it away from the bedside. The patient, who was group O, received 4 units of group A red cells. Over the next 4 days his haemoglobin fell to 40g/L and he became jaundiced. He died 3 weeks later from metastatic malignancy.

Case 2 Reluctance to take a further sample puts patient at risk

An on-call BMS received an urgent telephone request for 2 units of red cells, and was informed that there was a sample already in the laboratory. In this small hospital the on-call BMS was also responsible for phlebotomy out-of-hours and was reluctant to take a further sample from the patient. He was unable to find a transfusion sample, but instead located a full blood count sample taken the previous day and labelled with the patient's details. In contravention of laboratory procedures he used this sample for pre-transfusion testing; crossmatching and issuing 2 units of group A blood. An acute haemolytic transfusion reaction occurred after the first 30ml of blood were transfused. A further sample was taken from the patient and the correct group was found to be O. The sample had been taken from the wrong patient. The wrongly transfused patient survived the episode. The BMS was dismissed.

Wrongly labelled samples

In 2 cases the sample was taken from the correct patient but labelled with the wrong details, resulting in mis-transfusion.

Case 3 Benefit of historical record lost by incorrect labelling

This patient had been previously found to have auto-antibodies and a reference laboratory had recommended R₁R₁ blood. The wrong surname was written on both the sample and request form and an emergency admission number was given instead of a hospital number. The only correct reference points were the first name and the date of birth. The laboratory was therefore unable to find any previous record of the patient that would have alerted them to provide phenotyped blood. The patient suffered no ill effects.

Case 4 Confusion on SCBU results in wrong transfusion

Two infants on a neonatal unit, Baby Bloggs and Baby Soap, had the same date of birth. Baby Bloggs required transfusion. The SHO labelled the request form and the sample with Baby Soap's details and verbally requested blood for Baby Soap. Mrs Soap's sample was used for pretransfusion testing. Group O RhD negative blood was selected. The baby suffered no ill effects. See also Case 10, Chapter 12.

Learning points

- Misidentification of patient samples can result in potentially fatal ABO incompatible transfusion; there may be no means of detecting the error further down the chain.
- Discrepancies of labelling may result in duplication of patient records and loss of valuable information.

Inappropriate transfusions due to sample errors, analytical errors, communication failures and prescription errors

In 29 cases this year, patients were unnecessarily transfused or over-transfused as a result of errors in blood sampling or testing, mis-communication or mis-documentation of haematology results. Eleven of these were dilute samples taken from 'drip arms' or allowed to settle in syringes. In two cases the laboratory suggested the possibility of a dilute sample but clinical staff nevertheless proceeded with transfusion.

There were six errors by haematology laboratories; two of which were wrong haemoglobin determinations, one a wrong fibrinogen estimation leading to unnecessary transfusion of cryoprecipitate and three were spuriously low platelet counts due to clots or clumping as a result of which patients received platelet transfusions. Again this year, a haemoglobin level in one case was wrongly determined from a blood gas analyser; four other wrong haemoglobin results were unexplained.

In 7 cases, haematology results were wrongly documented or misinterpreted; in three of these the white cell count was taken to be the haemoglobin level.

One patient with sickle cell disease was transfused on the basis of wrong clinical advice from a specialist nurse at another hospital. In one case FFP was requested for and transfused to the wrong patient.

Three paediatric patients were over-transfused because of wrongly calculated prescriptions; these cases are discussed in chapter 12. One of these was also a laboratory error as adult red cell units were selected for an 18 month old child.

One adult patient (case 8) suffered major morbidity and required venesection as a result of overtransfusion.

Case 5 Laboratories should not accept unsuitable samples

An elderly male was admitted for investigation of chronic diarrhoea. A blood sample was sent to the haematology laboratory for a full blood count; the laboratory reported the result but queried whether the sample was dilute and requested a repeat. No repeat sample was sent; 6 units of blood were crossmatched and transfused. Post transfusion the patient was polycythaemic, but suffered no clinical ill effects.

Case 6 Poor sampling technique starts a series of errors

A post-operative blood sample was sent from a patient following repair of a fractured neck of femur. The haematology laboratory reported a Hb of 39g/L. The ward sent a nurse to the blood bank with instructions to collect uncrossmatched 'emergency O negative' blood. Because of an earlier refrigerator breakdown, the hospital blood stock was kept in the same refrigerator as blood for issue; the nurse removed 2 units of group O RhD negative blood from stock instead of taking blood designated and labelled for emergency issue. It was later realised that the low Hb level was incorrect due to poor sampling technique and the patient had not required the transfusion.

Case 7 Do the results match the clinical picture?

A male patient (age not given) was transfused with 8 units of red cells on the basis of a Hb of 23g/L. The patient was not bleeding and his clinical condition is not recorded. Post transfusion his Hb level was 188g/L. The cause of the spurious Hb result could not be determined. The patient survived with no ill effects.

Case 8 Post-transfusion increment should be monitored

A female adult patient of small stature was admitted with haematuria and Hb estimation was 63g/L. Four units of red cells were transfused, following which the Hb was 166g/L. A doctor failed to note the post transfusion Hb and prescribed a further 4 unit transfusion. Following this the Hb was 205g/L and the patient was noted to be hypertensive. Venesection was carried out daily for 3 days. The patient survived.

Case 9 Wrong Hb leads to unnecessary surgery

A young woman was admitted as an emergency with acute abdominal pain. A full blood count was done and a low Hb (level not given) was noted. As a result, a provisional diagnosis of ruptured ectopic pregnancy was made; the patient was transfused with 2 units of blood and a laparotomy was carried out. When no evidence of bleeding was found, a repeat sample was sent for full blood count and found to be normal. It was then realised that the first sample had been taken from the 'drip arm'.

Learning points

- Procedures for blood sampling must state that samples must not be taken from a 'drip arm'.
- A decision to transfuse must take account of clinical findings as well as laboratory results.
- Unexpected laboratory results should be reviewed and confirmed by a repeat sample. Haematology laboratories should not issue unvalidated results.
- Robust procedures must be in place in all clinical areas for recording telephoned results.
- Blood gas analysers are not suitable for haemoglobin estimation.

Failure to meet special requirements (107 cases). Better communication is urgently needed

One hundred and seven patients received blood components that did not meet special requirements, accounting for 31% of IBCT cases. The majority (88/107) involved errors at the request stage, though in 14 of these cases the requester was not aware of the special requirement as the patient's care was shared with another hospital who had not communicated the necessary information. In 39 cases the laboratory failed to select the appropriate component – these are further discussed in the section on laboratory errors.

Of these 107 events, 81 involved a patient at risk of TA-GVHD, for whom there was a failure to provide irradiated components. Fortunately there was no case of TA-GVHD and it is likely that leucodepletion of cellular components offers some protection, though gamma-irradiation remains the only reliable means of preventing this universally fatal complication.¹⁷ The commonest indication for irradiation (46/81) was treatment with a purine analogue.

Other 'special requirements' which were not met included CMV negative components (19, including 10 which should also have been irradiated), methylene blue (MB) FFP for children (6), components suitable for neonates (4), antigen negative blood for patients with known antibodies (2), components for patients post-ABO mismatched marrow transplant (2) and K-negative blood for young females where this is hospital policy (3).

One patient who had predeposited autologous blood for elective surgery was transfused with allogeneic blood because of multiple communication failures.

Case 10 Lack of awareness of guidelines puts patient at risk

A 66 year old male patient received fludarabine for chronic lymphatic leukaemia. The ward staff were unaware of the indication for irradiated blood components and so the laboratory was not informed. Over a 5 month period the patient received 13 units of unirradiated red cells.

Case 11 Failure of communication in shared care

A 14 year old male was admitted for an open lung biopsy following which he bled and required transfusion. He had previously received a stem cell transplant in another hospital in the same Trust, but there was no facility to link the two transfusion laboratory computer systems and the requester was not aware of the previous history. Non-irradiated red cells were given.

Case 12 No notice taken of an informed patient

An elderly male patient was admitted to hospital A with an ischaemic foot. He informed the ward staff that he required regular transfusion with 'special blood' at hospital B. The ward confirmed with the transfusion laboratory at hospital B that he had an anti-ANWJ but this information was not passed on to the laboratory at hospital A who were undertaking pre-transfusion testing. The antibody screen was negative and 3 units of red cells were issued electronically and transfused. The patient had a rise in temperature and a raised bilirubin, and died 8 days later from bronchopneumonia.

Case 13 Lack of effective IT 'flagging'

A young woman received an out-of-hours transfusion for iron deficiency anaemia. The clinical indication for urgency is not apparent from the report. The hospital had a policy of providing K-negative blood for women of child-bearing age, but the on-call BMS selected 4 units of red cells, one of which was K-positive. There was no 'flag' on the laboratory IT system to alert the BMS to the requirement for K-negative blood. The patient later became pregnant and on routine antenatal screening was found to have developed anti-K. Fortunately her partner was K-negative.

Learning points

- Robust systems are needed to ensure that patients at risk of TA-GVHD receive irradiated cellular components. The pharmaceutical industry and hospital pharmacists have important roles to play.
- There must be effective communication when patient care is shared between hospitals, to ensure that relevant information is available to all concerned.
- There is a need for education regarding guidelines and policies on special transfusion requirements.
- Patients should, wherever possible, be educated and empowered regarding their special requirements and staff should take note of information from patients.

Hospital Transfusion Laboratory Errors n=183

There were a total of 183 errors in this category occurring in 155 case reports. These are a diverse and complex group of problems; [a breakdown of types of errors is on the SHOT website.](#)

In 122/348 (35%) of all IBCT cases the primary error occurred in the hospital transfusion laboratory.

There were 118 reports of laboratory errors in which information was provided on the time the error took place.

69/118 (58%) were during normal 'core' working hours

49/118 (41%) were outside of core hours, either on-call or on a shift system

Preliminary analysis of a workload survey undertaken by SHOT in 2004 indicates that only 21% of all transfusion laboratory work is undertaken outside of 'core hours'. Further scrutiny of these data is required but there appears to be evidence to support the impression gained from this and previous SHOT reports that errors are more likely to occur outside core hours.

Wrong ABO group determination – a major danger area and staff under pressure

These 17 cases, in which patients were put at risk of potentially fatal ABO haemolytic transfusion reactions, resulted from selection of the wrong sample for testing (8 cases), interpretation or transcription errors (9 cases). As a result, 6 patients received ABO incompatible red cells and one incompatible FFP. Two patients suffered major morbidity, both survived. One patient died from injuries.

Wrong sample for ABO grouping

In these 8 cases (including 2 'paired' cases involving 4 patients) wrong ABO group determinations resulted from blood grouping using the wrong patient's sample. Four patients received ABO incompatible transfusions; 2/4 suffered major morbidity, but both survived.

A further sample transposition (involving 2 patients) was reported in which both patients were fortuitously Group O RhD positive.

Cases 14 and 15

Bert Fry required an elective transfusion but blood was requested out of hours. Emma Carter was admitted as an emergency following a miscarriage and required urgent transfusion. Neither patient was known to the laboratory. The on-call BMS inadvertently transposed the two samples on the bench. Fortunately, because of stock levels, he allocated group O RhD negative blood to Bert Fry, whom he had grouped as A RhD negative but was in fact B RhD positive. Emma Carter, whose correct group was A RhD negative, was grouped as B RhD positive and given 2 units of B RhD positive red cells. She suffered a haemolytic transfusion reaction and required anti-D immunoglobulin (Ig) and exchange transfusion.

Cases 16 and 17

Two patients required elective transfusion following cardiac surgery. The BMS labelled gel cards for both patients but transposed the samples and added the wrong patient serum and cells to the reagents. As one patient was group A RhD positive and one group B RhD negative, both received an ABO incompatible transfusion which in one case was also Rh incompatible. In addition, the patient who was B RhD negative also had an anti-E but did not receive antigen negative red cells. Although a whole unit of incompatible blood was transfused to both patients, neither suffered serious morbidity. The laboratory has since changed its procedures.

Right sample but wrong ABO group – manual methods are inherently unsafe

The cases in which the right sample was tested but the wrong ABO group was obtained are striking in that all involved a manual method and the result was either misread or incorrectly entered into the computer system. Only 5/9 cases appeared to be clinically urgent. In 5/9 cases the BMS did not work regularly in the transfusion laboratory or was relatively inexperienced in transfusion work. Because of the importance of these cases, all are summarised in table 2 below.

Table 2

Manual methods leading to wrong ABO groups

Case 18	RTA, Massive tx during day but a BMS not normally working in transfusion. Misread manual ABO group. 2 units ABO incompatible blood given before error realised. Patient died from injuries.
Case 19	RTA, uncrossmatched group specific blood requested. An inexperienced BMS misread manual group, checked by senior BMS but error not recognised. ABO incompatible blood given. Patient survived.
Case 20	Elective transfusion but testing undertaken outside core hours by BMS not working regularly in transfusion laboratory (shift system). Manual input of results. AB recorded as A.
Case 21	Premature infant, blood requested out of hours. Grouped as A using a manual technique, later found to be AB.
Case 22	Routine request but testing done by BMS not normally working in transfusion laboratory. An incorrect batch number had been entered on a plate reader so results could not be transferred electronically and were being entered manually. Patient's results entered as O RhD negative, instead of A RhD positive.
Case 23	RTA, blood required urgently out of hours. Testing done by on-call BMS regularly working in blood bank. Rapid manual method used, reactions misinterpreted. Patient group B, grouped as O.
Case 24	FFP requested to cover an elective procedure. Group done out of hours by on-call BMS who regularly worked in transfusion. Manual technique used - wrong group recorded (A instead of B). ABO incompatible FFP given. No adverse effect.
Case 25	Urgent request out of hours. On-call BMS not normally working in transfusion laboratory. Manual tube technique – results incorrectly documented and hence misinterpreted. Patient grouped as O instead of A.
Case 26	Urgent request for patient in theatre. Patient manually grouped as O, later found to be A. Details of error not clear.

Rh D group difficulties

Twenty-six errors in determination of RhD groups were reported. Of these, 16 resulted in administration of unnecessary anti-D Ig (see below). Six of these cases related to weak RhD groups, highlighting the pitfalls of RhD group determination. It is debatable whether these should be regarded as errors as appropriate reagents were used and it must be accepted that, due to the limitations of the technology, some laboratories will group weak RhD groups as positive and some as negative.

Eleven errors (RhD negative patients grouped as RhD positive) resulted in inadvertent transfusion of RhD positive red cells to RhD negative patients, 4 of whom were young females of potential child-bearing age, at risk of haemolytic disease in future pregnancies. One 12 year old female transfused following head injury underwent an exchange transfusion.

An additional wrong RhD group resulted from the wrong patient's sample being selected in the laboratory for grouping. (case 32 below)

Case 27 Patient protests ignored

A 42 year old female patient underwent reconstructive surgery following mastectomy, following which she required urgent transfusion. No previous sample had been sent for grouping. Pre-transfusion testing was carried out urgently by a BMS not normally working in transfusion. Manual ABO and RhD groups were carried out and results manually recorded. No reverse group was performed. The patient's RhD group was incorrectly determined as positive and Group O RhD positive blood was crossmatched and issued. The patient was aware that she was RhD negative and queried the group of the transfused blood, but was reassured by a nurse.

Case 28 Wrong RhD group on cord sample from direct antiglobulin test (DAT) positive infant

Following delivery by a RhD negative woman, a cord sample was sent to the laboratory for RhD typing. The infant was DAT positive and the BMS had difficulty in interpreting the cord RhD group. To 'be safe' he issued anti-D Ig. There was no clinical urgency and the results could have been reviewed by a more senior member of staff the following day. The infant was in fact RhD negative.

Case 29 Historic RhD group unavailable because of numbering discrepancy

A male patient was admitted through A&E with gastrointestinal bleeding. An on-call BMS undertook blood grouping but grouped the patient as RhD positive, when in fact he was RhD negative. The patient had been grouped previously but because he was allocated an A&E number the historical group was not available.

The proposed corrective action by the laboratory did not appear to include changing the patient 'look-up' procedures.

Antibody screen or ID errors and crossmatch errors – experienced support is needed to resolve complex cases

Fifteen cases were reported in which there were technical or clerical errors in antibody screening, identification or crossmatch. As a result 11 patients received incompatible red cells of whom 2 suffered haemolytic reactions. Six cases involved multiple errors. Again it is of note that 7/15 of these instances occurred out of core hours and 5/15 were urgent transfusions. Four of the cases involved a BMS not normally working in the transfusion laboratory. Seven cases were missed antibodies, in another three full pretransfusion testing was wrongly omitted. In 2 instances, blood was labelled as compatible and placed in an issue location pending resolution of serological problems - not surprisingly the blood was collected and transfused. Two BMSs were disciplined as a result of errors.

An additional 2 cases were reported in which pre-transfusion testing was carried out using a sample which had been stored for longer than recommended by guidelines.

Case 30 A complex serological problem out of hours

Blood was requested out of hours for a 'routine' transfusion. The on-call BMS did not normally work in the transfusion laboratory. The antibody screen was positive, however the BMS wrongly interpreted it as due to 'non-specific IAT antibodies' despite a negative IAT control. He crossmatched and issued apparently compatible blood. The following day further investigations showed an anti-S and anti-Kp^a. Two of the transfused units were S positive. The patient had a poor haemoglobin increment. The BMS was suspended from on-call duties.

In a similar case the BMS contacted the ward and agreed to delay the transfusion until the next day so that the positive antibody screen could be resolved. However he crossmatched and labelled the blood and placed it in an issue location – it was collected and transfused.

There are lessons to be learned from all the individual cases reported under these headings, - short vignettes can be found on the SHOT website.

Special requirements not met or inappropriate blood component selected – many preventable by better IT

Laboratory errors in 39 cases related to failure to meet special requirements. Of these, 22/39 patients were put at risk of TA-GVHD by failure to provide irradiated components. One patient's stem cell harvest was delayed as a consequence.

In 29/39 cases, the failure could have been prevented by an effective 'flag' on the laboratory IT system. One laboratory had lost its 'flags' when a new IT system was installed, resulting in 2 cases of failure to irradiate, and computer breakdown caused a further 3. In 9 cases laboratory staff had not updated the computer system. In one case the BMS ignored a computer 'flag' and in 5 the wrong component was selected by the BMS.

An additional seven cases were reported in which the patient's previous transfusion history was unavailable resulting in failure to provide suitable antigen negative blood. One laboratory had a paper record system; in the other 5, use of a different patient number meant that the historic record was not retrieved. Two of these patients suffered haemolytic transfusion reactions due to anti-Fy^a.

These cases highlight the need for laboratory IT systems to be able to search on a limited dataset and to provide effective 'flags' for patients with special transfusion requirements. There must be robust back-up systems in place for computer down-time, both planned and unplanned.

Case 31 Previous history not available from paper record system

A patient with thalassaemia major required elective transfusion. The laboratory was not computerised and no previous records were found in the paper filing system. Antibody screen was negative and the transfusion was uneventful. It was subsequently discovered that the patient had anti-K, undetectable for the past 3 years. When next investigated a strong anti-K was found.

Eight additional cases were reported in which laboratory staff selected components which were unsuitable for a variety of other reasons; 3/8 were for paediatric patients; 5/8 patients suffered some morbidity.

Telephone requests must be fully documented

Two almost identical reports were received in which telephone requests were incompletely documented in the laboratory, resulting in the wrong patient's sample being selected for pre-transfusion testing. In neither case was the transfusion urgent. In both cases there were 2 patients on the same ward with similar names, and both the laboratory and the ward failed to check the full details. Fortunately in both cases the blood given was ABO compatible. One of these cases is described in detail below.

Case 32 Don't rely on name alone for identification of samples or patients

Edith Watt and Edith Watts were on the same orthopaedic ward. Neither had been grouped previously. Their serum samples were adjacent in the laboratory storage rack. The laboratory received a telephoned request for blood for Edith Watt who was going to theatre for repair of her fractured neck of femur. The request was not documented in the laboratory. The BMS picked out Edith Watts' sample and used it to crossmatch blood which he labelled with Edith Watts' name, date of birth and hospital number. The nurse collecting blood for Edith Watt did not notice the discrepancy, nor did the 2 nurses who administered the blood. Edith Watt was not wearing a wristband and her notes were not available. She was group O RhD negative and received blood which was group O RhD positive.

In the following remarkable case no fewer than 5 individuals failed to spot the discrepancy between patient details on the pack and on the patient wristband.

Case 33 'Same name' coincidences must be expected

A patient was admitted to St Elsewhere's with a ruptured abdominal aortic aneurysm. The ward telephoned the laboratory requesting Group O uncrossmatched blood. The laboratory had previously received a sample for grouping from another patient with exactly the same name, who was Group A. The BMS, recognising the name but without checking the date of birth or hospital number, issued 4 units of uncrossmatched group A blood labelled with the date of birth and hospital number from the previous request. Two nurses gave the first unit without noticing the discrepancies. The patient was transferred to Large University Hospital (LUH) with a nurse escort taking with her the remaining 3 units of blood. On arrival in A&E, the nurse from St Elsewhere's together with a nurse from LUH gave the second unit without checking against the wristband. The patient was taken immediately to theatre where the anaesthetist gave the third unit, again without checking. Only when the fourth unit was given was the discrepancy noticed. The patient was found to be group O. He died on the operating table; the incompatible transfusion was not thought to have contributed to his death.

Stock control failures

In 27 cases failure of laboratory stock control procedures contributed to transfusion of a blood component which had expired (21 units of red cells and 1 FFP) or had been out of temperature control. IT systems are available to aid stock control and prevent issue of expired units from blood banks and satellite refrigerators.

Learning points from laboratory errors

- Laboratory staff working out of hours and/or under pressure are prone to make errors and must be supported by robust procedures and technology.
- Staff must not be required to work beyond their level of competence or experience.
- Procedures for rapid testing are more error prone than routine automated procedures and should only be used when there is clinical urgency.
- Patient name coincidences will happen and systems must be in place to protect against the consequences.
- Verbal communications are a potential source of errors and must require the same points of identity as written requests.
- Transfusion laboratory stock control procedures should ensure that expired units are cleared from issue locations. Laboratory IT systems must not allow expired units to be issued.
- Transfusion laboratory IT systems should provide effective 'flagging' of special requirements and alert staff to select appropriate components.

Errors in the collection and administration of blood components (n=232)

There were 232 errors in collection and administration of blood components in 187 cases.

In 36% of reported cases the primary error occurred at this stage of the transfusion process.

Of the 176 cases in which the time of the transfusion was reported, 65/176 (37%) took place between 8pm and 8am. It is of note that of the 33/176 (19%) transfusions started between midnight and 8am, 16/33 were stated to be 'routine'.

There were 156 instances of failure of the bedside checking procedure, which was again the most common error in the transfusion process. In 21/156 cases, this was the primary error, resulting in wrong transfusions being given. In 10 of these cases there were 2 patients being transfused simultaneously on the ward; four 'paired' reports were received.

In 45 cases a wrong blood component was collected from the hospital storage site and the error was not detected at the bedside. It is notable that 10 of these cases related to acutely bleeding patients undergoing urgent or massive transfusions in critical care situations (operating theatres, recovery suites, A & E departments, intensive care units or delivery suites).

In 135 cases, the bedside check failed to detect an error earlier in the transfusion chain; in 24 of these an expired unit was transfused. System failures included checking blood against documentation away from the bedside, absence of identification wristbands and in some cases complete omission of the bedside identification check.

Cases relating to children are also discussed in chapter 12.

In one case blood was delivered directly to A&E by the blood service and transfused without reference to the transfusion laboratory. In another a label became detached from a platelet pack and was re-attached to the wrong unit.

Outcomes of collection and administration errors

Twelve patients received ABO incompatible transfusions. Two of these patients died from massive bleeding, the incompatible transfusion was not thought to have contributed to their deaths. A further 2 patients suffered major morbidity as a result of acute haemolytic transfusion reactions.

Collection of incorrect component (n=45)**Table 3****Collection errors according to grade of staff involved and whether or not a formal check was made at this stage**

GRADE OF STAFF	FORMAL ID CHECK		
	Yes	No	Unknown
Qualified nurse / midwife	5	6	5
Unqualified nurse / midwife	2	0	1
Porter	5	5	0
Locum / agency	1	2	0
Qualified ODA	0	3	0
Unknown	2	2	1
Other*	1	3	1

*1 x Auxiliary nurse, 1 x Unqualified ODA, 1 x Anaesthetist, 1 x Ward clerk, 1 x SHO

The recent National Comparative Audit of Transfusion³ has demonstrated poor practice in the administration of blood at the bedside. The cases described here are a direct result of unsafe practices such as those identified in the audit, and initiatives to improve this area of practice are urgently needed.

Case 34 Two patients, same surname – a well known pitfall and 2 similar cases

Joe Soap, who was O RhD negative, required an urgent transfusion for bleeding oesophageal varices. There was another patient (Fred Soap) with the same surname on the ward for whom blood had also been crossmatched. Fred Soap was O RhD positive. Fred Soap's compatibility form had been stuck in Joe Soap's notes. An agency nurse was sent to the blood bank to collect blood for Joe. She collected a unit of Fred's blood which was then checked against Joe's notes but with reference to Fred's compatibility form. No bedside check was carried out.

A nurse noticed the discrepant name when taking down the empty bag.

Case 35

David Archer and Tony Archer were patients on the same ward and blood was crossmatched for both. David was O RhD positive and Tony was A RhD positive. The porter collecting blood for David removed a unit of Tony's blood and Tony's compatibility form. Nursing staff checked the details on the bag label against the (wrong) form, which was signed and placed in David's notes. David was not wearing a wristband and no identity check was done. The transfusion was stopped when he developed a fever, but only when the laboratory came to investigate the reaction was the ABO incompatibility realised. He survived the event.

Case 36 No light shed on wrong blood

A patient (group B RhD positive) was undergoing endoscopy in theatre for acute upper gastro-intestinal bleeding. A unit of group O RhD positive blood intended for another patient was collected from the theatre satellite refrigerator. Because the theatre was in semi-darkness for the endoscopy, the anaesthetist was unable to read the label and administered the blood without checking.

Case 37 Wrong blood given to patient in the intensive care unit (ICU) and delay in recognising an acute reaction

This case was particularly well investigated and a number of errors was identified. The patient, who was being treated in an intensive care unit for oesophageal carcinoma, received an ABO incompatible transfusion resulting in major morbidity but he survived. The transfusion was elective but was undertaken in the evening, pre-transfusion testing was done by an on-call BMS. A porter was sent to collect the blood, having been given only a surname (verbally) without any documentation. He collected the wrong unit from the blood bank refrigerator and did not correctly log the unit out. Two qualified nurses checked the unit against a compatibility form but did not check it at the bedside. Moreover the blood was held at room temperature for over 30 minutes before the start of transfusion. The patient developed fever, chest pain and haemoglobinuria but observations were not recorded at appropriate intervals and the transfusion reaction was not recognised until almost a whole unit had been transfused.

Failure of bedside checking procedure (n=156)**Table 4****Grades of staff involved in bedside incidents**

Grade of Staff	Number of cases
Qualified nurse & qualified nurse	98
Qualified nurse only	21
Qualified nurse & unqualified nurse	6
Qualified nurse & doctor	5
Qualified nurse & locum / agency	4
Doctor only	3
Doctor & doctor	2
Doctor & qualified ODA	2
Unqualified nurse & Unqualified nurse	1
Locum / agency only	1
No response	13

Cases 38 and 39 Why give non-urgent elective transfusion at night?

Two patients on an oncology unit required elective transfusions. Freda Fry was O RhD positive; Linda Snell was B RhD negative. The two units of blood were collected after midnight from the blood bank and checked on the ward away from the bedside. The units were inadvertently transposed and transfused to the wrong patients. Freda Fry suffered a severe acute haemolytic reaction after the first 50 ml of transfusion and required admission to ICU. She later recovered. Linda Snell's transfusion was stopped; she suffered no ill effects.

Cases 40 and 41 Patients in adjacent beds in A&E given one another's blood

These 2 patients were in adjacent beds in an A&E department at night. Both required transfusion. One was O RhD positive, the other one A RhD positive. It is not known whether they were wearing wristbands. Two units of blood were inadvertently transposed and given to the wrong patients. A nurse noted the discrepancy and the transfusions were stopped, neither patient suffered any ill effect.

Learning points

- Name coincidences are a source of error here as at other stages of the transfusion process and must be guarded against by full positive identification at every stage.
- In emergency situations safety must not be compromised for expediency.
- The final patient identity check must be done at the bedside against an identification wristband or equivalent attached to the patient. No other form of checking is acceptable under any circumstances.
- Transfusion should not take place at night unless clinically indicated.

Transfusion of 'unsafe' units – incorrectly stored or expired

Forty-three reports were received of inappropriate handling of blood components. These included 21 units of red cells transfused past their expiry date. All of these involved a stock control error by the laboratory (2 relating to satellite refrigerators) plus failure to check the expiry date at the bedside. There were 12 instances of red cells out of temperature control in clinical areas. In 4 cases this involved blood which was being transferred between hospitals. Ten miscellaneous handling errors included FFP stored at room temperature on a platelet agitator in a clinical area; platelets stored in a satellite refrigerator; an irradiated neonatal unit returned to the laboratory for discard and taken by an SHO and FFP issued past its expiry date by a BMS.

Learning points

- The pre-transfusion checking procedure must include a check of the expiry date of the component.
- Hospital transfusion teams must collaborate to ensure that procedures are in place for safe transfer of blood between hospitals.

Errors originating at the supplying blood centre

There were 10 errors by 7 blood centres. Errors included;

Failure of screening procedures to detect a strong anti-Fy^a in an apheresis platelet donor resulting in passive transfer of antibody sufficient to cause a positive antibody screen.

Failure to detect a high titre haemagglutinin in red cells labelled as suitable for neonatal transfusion resulting in accelerated red cell destruction in a group B infant.

Two instances in which a verbal report by a reference laboratory was inconsistent with the final report. In one case this resulted in failure to select antigen negative red cells; in another anti-D was inappropriately administered to a patient with a weak D.

Provision of RhD positive platelets when RhD negative had been requested for a RhD negative patient - this error was not detected by the hospital laboratory or at the bedside.

An ad hoc delivery of Group O RhD negative blood directly to an A&E department instead of to the transfusion laboratory. A doctor transfused the blood.

Failure to provide CMV negative components.

Errors in anti-D administration

SHOT has not actively encouraged reports of incorrect administration of anti-D Ig, but nevertheless each year reports of such events are received. This year there has been a reduction in the number of anti-D errors reported.

As with other IBCT reports, there are errors at all stages of the process, including patient identification, laboratory errors, incorrect serological reasoning in the laboratory and by clinical staff. The majority of errors are of commission and we receive few reports of errors of omission, which are likely to have more serious clinical consequences.

This year 26 errors were reported in 24 cases, of which 16 related to incorrect or equivocal RhD grouping in laboratories.

Table 5
Anti-D errors

Type of error	Number
Misunderstanding of guidelines by midwife	3
Anti-D given to wrong patient	3
Late administration of anti-D Ig (>72hrs)	2
Patient already sensitised, misinterpreted by laboratory	2
RhD grouping error – cord sample	5 (2 due to reagent problem)
RhD grouping error – maternal sample	5
Weak RhD group (includes 1 reference laboratory)	6

Case 42

The wrong notes accompanied a patient to theatre for a caesarian section. Anti-D Ig was given on basis of historical group in (wrong) notes without sending a confirmatory sample.

Procedural review

Whilst recognition, reporting and investigation of incidents serves to identify flawed systems, full benefit can only be gained from incident reporting if events are carefully analysed to determine root causes and contributory factors. Much has been written on the subject of root cause analysis and [a retrospective analysis of three cases reported last year is published on the SHOT website](#). HTTs and Transfusion Committees have a crucial role in ensuring that the loop is closed following an adverse event and that opportunities are taken to use such incidents as learning opportunities.

In a number of cases the 'corrective action' consisted of the addition of checking steps to processes, thus making them more complex. Staff are more likely to follow correct procedures if they are simple and straightforward and opportunities should be taken to review and revalidate processes when errors have occurred.

Disappointingly, an element of blame was apparent in many of the accounts of events. One BMS was dismissed, two were disciplined and others were removed from on-call rotas. Blame was also apportioned to some nurses, though not to medical staff who made errors. There still needs to be a shift of emphasis away from individual blame if incidents are to be fully shared and lessons learned from them.

COMMENTARY

- The number of inappropriate transfusion reports due to poor blood sampling techniques remains an area of concern. In addition to patient identification errors, these events may result from performing venepuncture on a limb into which an intravenous infusion is being given, inadequate filling of the sample tube or failing to mix the sample in the tube appropriately. These practices can cause spurious or incorrect laboratory results that can result in incorrect or inappropriate requests for blood components. Patient identification errors at this stage are particularly hazardous as they may be undetectable.
- Errors are more likely to occur under exceptional circumstances, particularly in clinically urgent situations when staff are under pressure and there is a high level of stress. Drills and practices of emergency procedures are effective in other environments and can contribute to the development of a 'safety culture' in clinical areas and in laboratories.
- Patients continue to be put at risk due to failure to communicate special transfusion requirements; most commonly the need for irradiated components in patients prescribed purine analogues. The use of this group of drugs is increasing and gamma-irradiation remains the only proven method of preventing TA-GVHD.¹⁷
- There are numerous examples of laboratory staff working under pressure, either when blood has been requested urgently, or out of hours, or both. It is of concern that, among errors likely to result in incompatible transfusion, 8/9 ABO grouping errors and 7/15 antibody identification or crossmatch errors were related to out-of-hours or urgent work. The increasing moves towards a 24/7 level of hospital activity and the pressures of other NHS initiatives exacerbate these stresses.
- Administration of blood at the bedside remains an important risk area, as demonstrated by events reported to SHOT and by the findings of the National Comparative Audit³. A co-ordinated initiative is needed to address this area.
- A disproportionate number of incidents involving infants has been reported this year. These are further considered in chapter 12. There is a need for education of staff in paediatric units and laboratories, in special transfusion requirements of children including volume calculation.

RECOMMENDATIONS

- Hospital risk management committees must ensure that all staff undertaking venepuncture for blood sampling must have received the necessary training and have their practical competency formally assessed and recorded. Blood samples should be taken from a free flowing venepuncture site, and the tube should be filled to capacity and inverted gently several times to adequately mix the sample and any anticoagulant. The person taking the sample must complete the tube label before leaving the patient, checking the details are correct with the patient and against the ID wristband or equivalent.

Action: Hospital risk management committees

- Hospital risk management procedures should include 'drills' for high risk situations such as massive transfusion, involving all relevant staff.

Action: Hospital risk management committees

- Prevention of TA-GVHD in patients receiving purine analogues is the responsibility of prescribers, but can and must be supported by the pharmaceutical industry and pharmacists and by suppliers of laboratory IT systems. All patients should receive an information card and leaflet and haematologists must ensure that there is an effective system of flagging special transfusion requirements in the laboratory. Referrals for shared care must include timely communication of all relevant information.

Action: Clinicians prescribing purine analogues and administering blood transfusion; HTTs; pharmacists, pharmaceutical industry; suppliers of laboratory IT systems

- Hospital blood bank laboratory staffing must be sufficient for safe transfusion practice. Hospitals must ensure that blood transfusion laboratories have adequate numbers of appropriately trained biomedical scientists to cover the 24-hour working day, including a core of permanent blood transfusion laboratory staff. Standards should be established for manpower appropriate to the level of workload and this should be subject to inspection.

Action: Clinical directors of pathology, professional and accrediting bodies

- Paediatric units undertaking transfusion must ensure that staff are educated in the special transfusion requirements of children. Laboratory IT systems should be regularly updated to support implementation of new guidelines.

Action: Paediatricians and laboratory staff responsible for transfusion of paediatric patients; HTTs

- The most important contribution which could now be made to the safety of blood transfusion would be an initiative to improve the safety of the bedside pretransfusion checking procedure. This will require investment in education and audit, and also in evaluation and implementation of suitable information technology. The CMO's NBTC has the necessary remit to take this forward.

Action: CMO's NBTC through regional and hospital transfusion committees: HTTs

5 Near Miss Events

Definition :

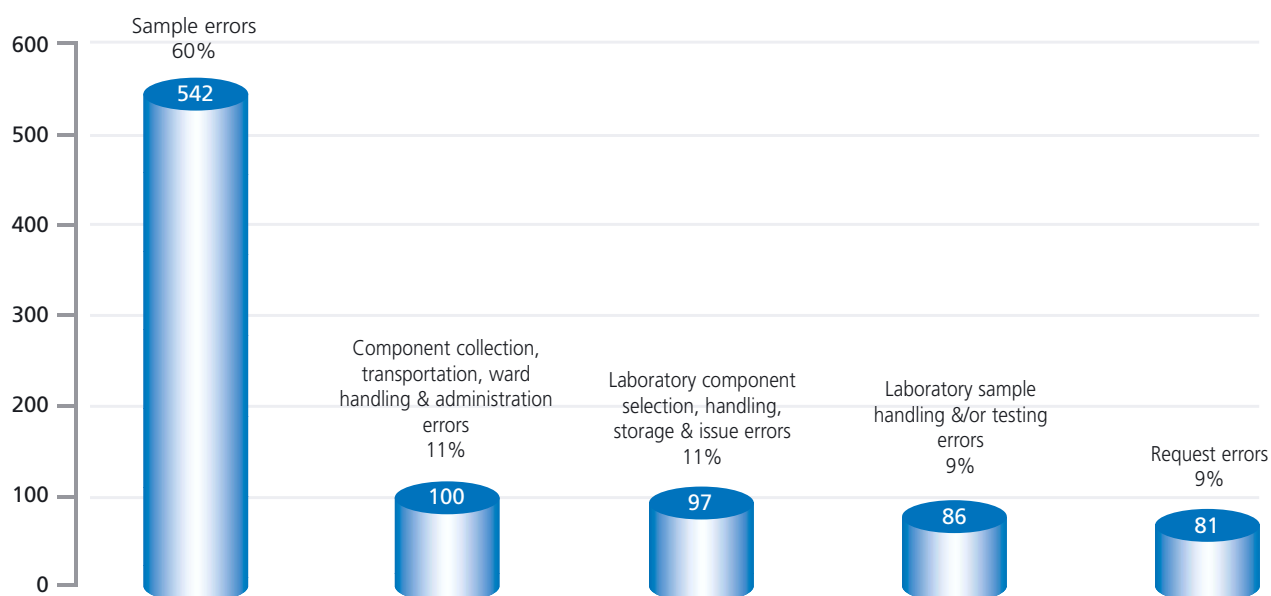
Any error, which if undetected, could result in the determination of a wrong blood group, or issue, collection, or administration of an incorrect, inappropriate or unsuitable component but which was recognised before transfusion took place.

The history and future of "near miss"

Following small pilot schemes first launched in 1997/98 and repeated the following two years, SHOT invited all UK hospitals to report "near miss" incidents beginning with the report year 2000/2001. The picture has been a consistent one showing errors made during phlebotomy to be by far the most numerous (50% in 2000/2001, 59% in 2001/2002 and 60% in 2003). Anecdotal evidence from reporting hospitals suggests that "near miss" events are frequent and common but there is demonstrable gross under-reporting. Last year, while overall reporting to SHOT was calculated to be 93%, "near miss" reports were received from only 41% of participating hospitals. The most likely explanation for this is that the large number of events witnessed makes reporting of them difficult to sustain. Since the pattern of events appears to vary little from year to year it would seem logical and advisable to move to a system of enabling hospitals to report their "near miss" events en masse rather than having to complete a single form for each event. We know that many hospitals report this way internally and we would like to find methods of sharing this information without increasing greatly the workload of already over-stretched laboratory staff. Many valuable lessons have been learned from the data we have collected so far but there seems little point in simply re-iterating the same messages particularly since we are probably seeing only the tip of the iceberg. The chapter this year then is considerably shorter than in previous years and aims to give an overview rather than an in-depth analysis of events we have reported on before.

For consistency, the categories and numbers of events reported this year are shown in figure 7.

Figure 7
Categories and proportions of "near miss" events



Category 1 : Sample errors (542 cases)

Once again sampling errors proved to be the most numerous comprising 60% of all "near miss" events reported. The majority of these errors were picked up from historical records on laboratory computers or by the vigilance of laboratory staff in carrying out double checks. Several of these events involved errors in haematology or biochemistry results which, although not strictly the responsibility of blood transfusion laboratories, would have resulted in unnecessary transfusions had they not been discovered in time. This is an important issue since there has been a large number of cases reported in the "Incorrect Blood Component Transfused" chapter which, unfortunately, were not detected in time. Many errors reported last year were consistent with those reported in earlier years. In particular the following types of error occur regularly and should be a priority for investigation and prevention :

- Samples in syringes, which are left unattended for a period and then dispensed into tubes without mixing.
- Dilute samples taken from "drip arms".
- Point-of-care (POC) testing variations.
- Labelling of samples remote from the patient.
- Pre-labelling of specimen tubes for RhD negative deliveries with subsequent confusion of tubes between mother and baby.
- Wrong addressograph labels used.
- Labels placed in wrong patients' notes.
- Poor patient identification using only one or two identifiers.

Category 2 : Request errors (81 cases)

A frequently reported problem in this category was a failure to notify the transfusion laboratory of the need for CMV negative and/or irradiated components. This is a commonly recurring theme both in "near miss" events and in full incidents and often indicates a need for improved communication between hospitals where patients are receiving shared care.

The majority of errors in this category were made by junior doctors, usually senior house officers, highlighting the need for education and training for medical staff requesting and prescribing blood components.

Category 3 : Laboratory sample handling / testing errors (86 cases)

A wide variety of errors was reported in this category consistent with previous years. It is interesting that many of these incidents were said to have occurred because the staff were either "very busy" or "under pressure" indicating the need for Trusts to review staffing levels or shift patterns. Most of these laboratory errors were recognised by the staff themselves retrospectively but not always before components had been issued.

Category 4 : Laboratory component selection, handling and storage errors (97 cases)

The majority of these reports related to poor housekeeping systems with evidence of poor practice in stock control of remote refrigerators. In addition there were several cases involving the issue of units close to expiry which were to be used for theatre cover at a later date. There were also several cases in which a refrigerator alarm had failed but this was not recognised by the staff.

Nine cases were reported in which the Blood Centre had provided the wrong specification of component to the hospital. The most worrying of these was one in which granulocytes were provided which had not been irradiated. The hospital BMS was unaware of the need for irradiation and issued the component to the ward. Fortunately the error was picked up at the pre-transfusion check.

Category 5 : Component issue, transportation and patient identification errors (100 cases)

Storage and transport problems accounted for 51% of errors in this category. Most of these involved storing units in inappropriate refrigerators, for example chemotherapy and drug refrigerators. Several cases were reported of blood being left out of temperature control for extended periods including 1 unit which was left on top of a locker for 12 days. The collection of an incorrect unit was another frequently reported error, this year comprising 31% of category 5 errors. Notably in 20 of these 31 cases the unit was collected by a porter and porters were also cited in 3 other category 5 incidents.

In one reported case the porter happened to meet the SPOT en route from the blood bank. He was found to have no documentation with him, had collected the wrong unit of blood and was planning to complete the collection slip retrospectively. In another case the porter collecting the blood had received no training and was unable to read English, and in a third, the person collecting the blood had forgotten her glasses!

Right blood to right patient

Each year there are a number of cases reported in which the patient receives entirely appropriate blood which was intended for them but which, nevertheless, had some element in the process which was wrong and which could, under different circumstances, have led to a serious transfusion error. It has always been difficult for SHOT to place these events appropriately. They do not constitute Incorrect Blood Transfused events since they are not covered by that definition. Nor can they really be defined as "near miss" since that definition requires that no volume of blood should have been transfused. They are, however, fairly frequent and warrant some discussion. It has been decided, therefore, to include them in the numbers of "near miss" events as a separate category and to try to amend the definition accordingly before the next reporting year. There were 29 such cases reported this year.

Problems in reporting

This year unforeseen technical problems with the SHOT database have meant that cases coming in to the office have not been reviewed in a timely manner. This has produced the unfortunate effect of cases being reported as "near miss" which were, in fact, full IBCT incidents. However, by the time these cases were ready for review it was too late to obtain the necessary information from hospitals which would have enabled us to convert them into IBCTs and report on them properly. These cases are, therefore, not counted in the numbers of either "near miss" events or IBCTs for this year. Reporters are asked to be particularly careful about not reporting IBCTs as near misses and to contact the SHOT office at any time if they have any doubt about a particular case. The one essential criterion to remember is that an event is not "near miss" by our definition if any volume at all has been transfused. The error must have been recognised before any blood component passed through the venflon. The "near miss" definition does not allow for reporting of events where, for example, a patient received a small volume of red cells which were intended for another patient but which was, fortuitously, fully compatible and the patient suffered no ill effects. These cases are defined as "Incorrect Blood Component Transfused" and must be reported on the appropriate form.

There were 6 such cases reported inappropriately as "near miss" which were, in fact, full IBCT incidents and these are summarised below. At the end of each case the reporter's rationale for reporting them as "near miss" is included and is intended to illustrate the sorts of false reasoning outlined above.

1. A patient on a coronary care unit was given 2 units of blood based on a Hb result of 98 g/L. Over the next 2 days there were widely differing Hb results for this patient ranging from 74 g/L to 138 g/L. A further 2 units were transfused in the meantime. It is thought that the discrepant results were due to dilute samples though this has not been fully established.

The case was reported as "near miss" because the patient suffered no ill effects

2. A patient due to go into theatre had Hb results in his notes which belonged to another patient. This result was used as an indicator for transfusion. Nursing and theatre staff questioned the need for the transfusion and discovered the error on investigation.

Reported as "near miss" because the transfusion was stopped after only a few mL had been transfused and the patient suffered no harm

3. A unit of blood was transfused to a patient 47 hours after the crossmatch had expired.

Case reported as "near miss" because the blood was crossmatched for the patient concerned

4. A transcription error in the laboratory led to incorrect patient details being used to group and crossmatch a unit of blood.

This was reported as "near miss" because the unit transfused was compatible

5. Prophylactic anti-D was issued by the laboratory and the ward informed that it was ready for collection. However the unit was not collected until 5 days later despite daily reminders by the laboratory staff.

Reported as "near miss" because the anti-D was given eventually

6. Anti-D was not given to a pregnant woman who was RhD negative and who had chorionic villus sampling (CVS) in an antenatal clinic. The consultant in the clinic wrote her blood group in the CVS book as RhD positive based on a verbal report by the patient.

This was reported as "near miss" because the patient had been given anti-D in a previous pregnancy

"Near miss" reporting 2004 and 2005

Discussions are underway concerning how to collect "near miss" data in the future. We are aiming to develop new systems in time for the start of reporting in 2005. Meanwhile we are continuing to accept reports on the current questionnaires and hospitals are encouraged to submit as many reports as possible. We know that some hospitals report their "near miss" incidents in bulk internally. Until the new systems are in place we would also encourage hospitals to phone the SHOT office for advice if they would also like to report these cases to SHOT. We will endeavour to find ways of handling bulk reports manually until new systems have been developed.

6 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 as these are covered in Chapter 4

This category accounted for 9.3% of non-infectious hazards reported and 9.1% of all hazards.

There were 6 outstanding reports from the previous reporting year for which 5 questionnaires were eventually received although on review one of these was, in fact, an incorrect blood component transfused and is now transferred to that section. The remaining 4 are included in the analysis. Forty-four valid initial reports were received and 39 completed questionnaires (including 4 from the previous year). The 9 outstanding questionnaires will be included in next year's analysis. An additional 12 reports did not fit the definition of ATR and have been withdrawn by the analyst.

This chapter highlights the main findings from 39 completed questionnaires.

There were 5 deaths in this group; 1 probably related to the transfusion, 1 possibly related to the transfusion and 3 unrelated to the transfusion. There were 2 instances of major morbidity and renal failure as a result of haemolytic transfusion reactions.

Gender (37 reports)

Male 21

Female 16

Age (38 reports)

Age range 3 months to 84 years

Median 66 years

Components implicated (39 reports)

Red cell - allogeneic 8

Red cell – post-operative salvage 1

Platelets 13 (8 apheresis units and 5 from pooled buffy coats)

Fresh frozen plasma 17 (all not viral inactivated)

Reactions in which red cells were implicated

There were 8 cases, with one death possibly related to the transfusion, and two cases of major morbidity. Six reactions occurred during the transfusion, 1 within 7 hours of completing the transfusion and 1 unknown. The following reactions were seen:

Table 6

Reactions in which red cells were implicated

Reaction type	Number of cases
Haemolytic or incompatibility reaction	4
Anaphylactic/anaphylactoid*	1
Allergic**	1
Unknown/unclassifiable	2

* anaphylactic/anaphylactoid (hypotension with 1 or more of: rash, dyspnoea, angioedema)

** allergic (1 or more of: rash, dyspnoea or angioedema **without** hypotension)

Haemolytic or Incompatibility Reactions

In 4 cases, there were features of haemolysis

Case 1

A 75 year old male with no previous transfusion history had a coronary artery bypass graft (CABG) performed, during which he bled excessively and was transfused with 14 units of red cells, 13 units of FFP and one unit of platelets. Within 7 hours of the procedure, the patient developed a fever, rigors, and chest pain. He became hypotensive, was noted to pass dark urine and was found to have a strongly positive DAT(IgG), hyperbilirubinaemia, spherocytes, haemoglobinuria, disseminated intravascular coagulation and deteriorating renal function that required dialysis.

The patient had two antibody screens pre-operatively. The first performed at the pre-assessment clinic was weakly positive and a provisional specificity of an anti-E was given on the basis of a positive reaction with one R₂R₂ cell. The patient's Rh phenotype was R₂r, the DAT was negative and an auto-E was questioned. The second antibody screen performed on admission was negative but he was crossmatched with E negative units. Post-operatively the patient's plasma contained a strong anti-E, reacting 5+ in IAT and anti-E was eluted from the red cells. These post-operative findings were confirmed by the reference laboratory and an auto-anti-E was again suggested to be responsible.

There are very few cases of an autoantibody being stimulated by transfusion, and the rapid response over a few hours is surprising. However, the finding that anti-E could be eluted from the E negative units transfused would support the hypothesis that this was an autoantibody.

Case 2

A 30 year old female was transfused 2 units of red cells on account of a post-partum haemorrhage and required 2 further units a few days later. During the second transfusion episode, she became febrile, dyspnoeic and was noted to be passing dark urine. She was subsequently found to have a positive DAT (IgG only), haemoglobinuria and deteriorating renal function and required dialysis and admission to ICU. Her pre and post-transfusion antibody screens were repeatedly negative using an automated DiaMed technique. These samples were referred to the Reference Laboratory who detected an anti-Jk^b and an anti-K in the pre-transfusion sample by papain IAT only, and confirmed that the implicated unit was Jk^b positive.

The reporting hospital has since amended its protocol for investigating red cell transfusion reactions to include additional techniques.

Case 3

An example of a patient with an anti-Do^a who as a result of two consecutive transfusions, experienced a delayed haemolytic transfusion reaction followed by an acute haemolytic transfusion reaction. The vignette is included in Chapter 7 (Delayed Transfusion Reactions).

Case 4

A 50 year old female with myelofibrosis required regular transfusion support. The patient had experienced a febrile reaction during a transfusion of 3 units of red cells approximately 3 weeks earlier but a decision was taken to continue the transfusion with chlorpheniramine cover. On the following occasion, the red cell transfusion was stopped after 50ml on account of rigors and a tachycardia and following the transfusion the patient was noted to have a raised bilirubin. She had a negative IAT antibody screen pre and post transfusion and the DAT was negative throughout. However when samples were referred to the local Reference Centre, the patient was found to have an anti-c+E together with a non-specific papain autoantibody in the pre-transfusion sample.

It is not known why these antibodies were missed and the reporting hospital has since amended its protocol for investigating red cell transfusion reactions to include the use of enzymes and low ionic-strength saline (LISS) tube techniques.

Anaphylactic/anaphylactoid reactions

One patient who was IgA deficient developed an anaphylactic reaction due to anti-IgA.

Case 5

A 70 year old male had an anaemia of chronic disease and was undergoing debridement of an infected foot. On the first occasion, after 86ml of red cells had been transfused, the patient developed dyspnoea with tachycardia and profound hypotension. He was successfully resuscitated and repeat testing of the pre and post transfusion sample revealed no red cell incompatibility and bacterial cultures were negative. Two weeks later, a further red cell transfusion was given with hydrocortisone and chlorpheniramine pre-medication. After one hour the patient developed severe rigors and the blood pressure rose from 134/80 to 206/120.

The transfusion was again aborted and the patient resuscitated with hydrocortisone and chlorpheniramine. At this stage the patient was tested for IgA deficiency and found to be IgA deficient with an anti-IgA antibody. Subsequent transfusions of washed red cells have been tolerated.

A severe allergic reaction should have been suspected after the first transfusion.

Reactions of unknown aetiology

Case 6

An 80 year old female, with a non-Hodgkin's lymphoma and previously untransfused, had a positive DAT(IgG only) but a negative red cell antibody screen (Ortho BioVue IAT). The patient was also reported to have an autoimmune haemolytic anaemia although no clinical details are available. Three units of red cells were issued electronically. During the third unit, the patient developed a fever, breathlessness, hypotension and a reduced level of consciousness. The transfusion was stopped and antibiotics were prescribed. The patient died two hours later. The patient had a negative antibody screen post transfusion and the units were compatible when retrospectively crossmatched.

No bacterial cultures were taken, a chest X-ray (CXR) was not performed and it is not clear whether any of the symptoms were related to the transfusion rather than underlying sepsis.

The reporting hospital now perform a serological crossmatch on patients with a positive DAT.

Case 7

A 20 year old male, who had undergone an orthotopic liver transplant 15 years earlier and who was known to have a warm autoimmune haemolytic anaemia had not required red cell support for several years. On the reported occasion, after an unspecified volume of red cells, the patient developed a fever, rigors, hypotension, nausea and vomiting. Pre-transfusion testing revealed a positive DAT (IgG only), and an autoantibody reactive in the IAT with no apparent specificity. No testing was undertaken to exclude underlying alloantibodies and no serological crossmatch was performed. The post transfusion sample again showed a strong autoantibody.

Subsequent red cell transfusions, given slowly, have been well tolerated.

Reaction to a unit of autologous salvaged blood

Case 8

An 84 year old male who had undergone a total knee replacement was transfused with unwashed red cells salvaged post-operatively. After 550ml had been given, the patient developed a fever, rigors and dyspnoea requiring bronchodilators and high dependency unit (HDU) admission. Bacterial cultures of both the unit and the patient were negative.

Filtered salvaged blood contains cytokines that may have been responsible for the reaction

Reactions in which FFP was implicated

There were 17 reports in this group, of which 15 occurred during the transfusion, and 2 within 2 hours. The following reactions were seen:

Table 7

Reactions in which FFP was implicated

Reaction Type	Number
Anaphylactic/anaphylactoid	8
Allergic	8
Unknown/unclassifiable	1

Anaphylactic/anaphylactoid

There were 8 patients in this category, all of whom recovered from the reaction. Seven occurred during the transfusion, and where information is available, started after 50-200 mL FFP had been given. The eighth case was noted within 30 minutes of completing the infusion.

Five cases had dyspnoea, of which one had a CXR performed (result unknown) and one had blood gases taken confirming hypoxia.

Four patients required adrenaline in addition to hydrocortisone and chlorpheniramine, of which 2 were also given bronchodilators. A fifth patient was given hydrocortisone and chlorpheniramine and a sixth oxygen alone. It is not clear what medication was prescribed for the remaining 2 patients.

Five of the 8 patients were investigated for IgA deficiency, with negative findings.

Four out of 8 FFP transfusions can be justified, (included in table 8 below).

Case 9

A 68 year old man on warfarin was scheduled for a colonoscopy and biopsy and had been asked to discontinue his anticoagulants three days before admission. On admission, the day before the intended procedure, his INR was 1.65 and he was prescribed FFP.

Within 10 minutes of starting the transfusion, the patient had developed an urticarial rash. He was seen within a few minutes by which time he had become hypotensive, BP 58/33, wheezy, developed rigors and lost consciousness. He required two IM injections of adrenaline, in addition to 200mg hydrocortisone, 20mg chlorpheniramine and crystalloids/colloids over 30 minutes to become haemodynamically stable. He was also given nebulised salbutamol and oxygen. He had a normal IgA level.

Allergic reactions (not anaphylaxis)

There were 8 patients in this group, all of whom were also dyspnoeic. 6 had a rash which was accompanied by angioedema in 2 cases. The remaining 2 had rigors in addition to dyspnoea.

No CXRs were performed. 4 were investigated for IgA deficiency with negative findings and there were no investigations performed in the remaining 4 who had all been previously transfused.

3 out of the 8 FFP transfusions can be justified (included in table 8).

Case 10

A 43 year old male with Crohn's disease, also on warfarin for a previous pulmonary embolus, was noted to have an infected Hickman line. He was scheduled for surgery 3 days later but was not informed to discontinue his warfarin. He was admitted 2 days before surgery and was found to have an INR of 2.9 and was prescribed FFP.

At the end of the first unit, the patient developed a rash, a swollen tongue, and became dyspnoeic with an oxygen saturation of 88%. He responded to hydrocortisone, chlorpheniramine and nebulised salbutamol. His IgA level was normal.

Unclassifiable**Case 11**

An 80 year old patient (gender not reported) was admitted with sepsis and disseminated intravascular coagulation. He/she was transfused with one pool of platelets followed by FFP. During the second unit of FFP the patient became breathless but had no other features of an allergic reaction. The unit was discontinued, the patient received hydrocortisone and chlorpheniramine and further FFP was transfused later at a slower rate without problems. Although a reaction to FFP could have accounted for the breathlessness, alternative explanations include fluid overload and the underlying sepsis.

Inappropriate use of FFP

Coagulation results are not available for some reports and these have been designated as possibly indicated. However, it is apparent that at least 5 of the 17 FFP transfusions were not indicated.

Table 8**Indications for FFP transfusion**

Category	Number patients	Indication given
Clinically indicated	7	TTP – 1 Massive transfusion – 2 Liver disease with haemorrhage – 2 DIC with haemorrhage – 1 Warfarin reversal - 1* (*INR >10, haematemesis, jaundice, abdominal pain ? for surgery)
Possibly indicated	5	Warfarin reversal, bleeding – 1 Perioperative bleed in the absence of massive transfusion – 4
Not indicated	5	Non-urgent warfarin reversal in absence of bleeding – 3 Liver disease in the absence of haemorrhage or intervention – 1 Enoxaparin (Clexane) reversal on account of bleeding at site of injections - 1

Reactions in which platelets were implicated

There were 13 reactions in this group, of which 11 occurred during the transfusion, 2 within 2 hours and 2 were recognised up to 8 hours following the transfusion. One patient died as a result of an anaphylactoid reaction and there were 3 other deaths unrelated to the transfusion.

Table 9**Reactions in which platelets were implicated**

Reaction Type	Number of cases
Haemolytic	2
Anaphylactoid (see text above)	1
Allergic	9
Unknown	1

Haemolytic reactions**Case 12**

A 31 year old male with acute lymphoblastic leukaemia had undergone an unrelated donor stem cell transplant. Both the donor and the patient were genotyped as group A₁. On day +8, the patient received platelets from a group O apheresis donor who had tested negative for high titre anti-A/B on ten occasions. Although the patient was asymptomatic at the time of the transfusion, within 24 hours there were features of haemolysis with a positive DAT, hyperbilirubinaemia, spherocytosis, a falling haemoglobin and deteriorating renal function. Dialysis was not required but the patient had delayed engraftment (>21 days) with neutropenia dependent upon granulocyte-colony stimulating factor. He went on to become polymerase chain reaction (PCR) positive for CMV on day +25 and died of CMV pneumonitis on day+40.

Retrospective manual testing of the apheresis donor demonstrated an IgM anti-A titre of >1:1024 (saline agglutination) and an IgG anti-A titre of >1:8192 (LISS tube IAT). Although the patient died from CMV pneumonitis, he received CMV seronegative blood components. The haemolytic episode however could have contributed to the delayed engraftment.

Case 13

A 3 month old female infant, group A Rh D negative, was born with a ventricular septal defect (VSD) and cardiac atresia and was being supported on extra-corporeal membrane oxygenation (ECMO). She had received large quantities of blood components over the previous 7 days and in the 24 hours leading up to the report had been given 7 aliquots of group O Rh D negative neonatal platelets due to a shortage of A Rh D negative neonatal platelets at the Blood Service. Within 24 hours haemolysis was noted with a free plasma haemoglobin of 316g/L. The DAT was positive and anti-A was eluted from the red cells. The baby subsequently died though not as a direct result of the haemolysis.

Anaphylactic/anaphylactoid reactions**Case 14**

A 72 year old male with aplastic anaemia, known to have cardiac impairment, had been treated with antilymphocyte globulin (ALG) but was still red cell and platelet dependent, requiring 2 pools of the latter on a weekly basis. After receiving 250mL of an apheresis platelet concentrate he developed a rash which initially settled with hydrocortisone but he went on to become hypotensive and dyspnoeic. The patient was resuscitated with antihistamine, hydrocortisone and adrenaline but suffered cardiac arrest, developed irreversible ventricular fibrillation and died.

He had a normal level of IgA and culture of the platelet unit was negative.

Allergic reactions (not anaphylactic)

Nine cases of allergic reactions were reported in patients who had all been previously transfused. All patients made a full recovery following treatment with antihistamines and in some cases, hydrocortisone.

Seven of the 9 reactions were accompanied by fever and in 4 of these, the units were sent for bacterial culture with negative findings.

Six were accompanied by transient dyspnoea and no chest X-rays were performed.

Two patients had no investigations performed.

Five patients were tested for HLA and/or human platelet antigen (HPA) antibodies and of these 2 were found to have HLA antibodies and 1 to have HPA antibodies. There is no information as to whether these patients were found to be refractory to random platelets or whether the reaction occurred prior to the development of refractoriness.

Two patients were tested for IgA deficiency with negative findings and 1 patient was additionally tested for mast cell tryptase and Am and Gm antibodies.

Unclassifiable**Case 15**

A 72 year old male with end-stage chronic lymphocytic leukaemia required red cell and platelet support. Towards the end of a transfusion of a unit of buffy coat derived platelets he developed a fever, chills, rigors and dyspnoea. A CXR was performed which showed upper lobe blood diversion and pulmonary oedema. He was treated with a diuretic, nebulised bronchodilators, oxygen and broad spectrum antibiotics. The platelet pool was not sent for culture but the red cells from the 4 donors were cultured with negative results. The patient's discharge was postponed but he later recovered.

The CXR findings were more in favour of left ventricular failure than TRALI but this does not provide an explanation for the fever and rigors. Bacterial contamination of the platelet preparation has not been satisfactorily excluded.

Response times

The majority of patients were seen as soon as possible by a doctor but a haematologist was not always consulted in the management of a reaction and a minority of incidents involving platelets were brought to a haematologist's attention.

Table 10**Time taken for patient to be reviewed by a doctor**

Response Times	Red cells (8)	FFP (17)	Platelets (13)
Stat	3	9	8
< 30 minutes	2	3	3
< 60 minutes		1	1
> 60 minutes			
Not available	3	4	1
Late reaction			
Total	8	17	13
Involvement of Haematologist	4	9	5

Changes made to procedures

Two laboratories that failed to detect red cell alloantibodies using their routine IAT technique now employ additional techniques for investigating haemolytic transfusion reactions.

The laboratory that employed electronic issue for a patient thought to have an autoimmune haemolytic anaemia has now reverted to serologically crossmatching blood for these patients.

Reporting of acute transfusion reactions**Table 11****Reporting of reactions to the Hospital Transfusion Committee, Hospital Laboratory and the local Transfusion Centre**

Reported to	Red cells (8)	FFP (17)	Platelets (13)
Hospital Transfusion Committee	7	14	13
Hospital laboratory	7	17	10
Transfusion centre	5	8	11

COMMENTARY

- The majority of ATRs (30/39) were due to FFP and platelets, as in previous years. 93% (26/28) allergic or anaphylactic/anaphylactoid reactions were due to these 2 components.
- It is apparent that FFP has a notable risk of causing an acute reaction and yet is often inappropriately prescribed, particularly when there is a non-urgent need for warfarin reversal.
- Two group A infants developed haemolytic transfusion reactions after receiving group O neonatal platelets, tested for high titre anti-A/B.
- Only 5/8 patients experiencing an anaphylactic reaction to FFP were investigated for IgA deficiency.
- Two patients with serious reactions to platelets had no investigations whatsoever. Although platelet concentrates pose the highest risk of bacterial contamination, cultures were only performed in 4/9 cases when the reaction was accompanied by a fever.
- Haematologists are not frequently involved in the management or investigations of suspected acute transfusion reactions which can lead to inappropriate diagnosis and treatment.
- Whilst there is no requirement to perform a DAT as part of routine pre-transfusion testing, samples from patients who are found to have an autoimmune haemolytic anaemia should be referred to a reference laboratory to exclude underlying alloantibodies.

RECOMMENDATIONS

- The BCSH guideline dealing with the investigation and management of acute transfusion reactions is awaited and emphasis should be placed upon the need for identifying underlying causes that will impact upon the choice of future component therapy.

Action: BCSH

- There is continued evidence of inappropriate clinical use of FFP, despite the availability of recently published BCSH guidelines¹² on appropriate use and existing recommendations for the management of warfarin reversal¹³. Further local audits and educational programmes should be encouraged through the Transfusion Committee network.

Action: Regional and hospital transfusion committees

- The recent BCSH transfusion guideline for neonates and older children⁹ states that group A recipients should receive group A platelets, but accepts that group O can be transfused as a second alternative provided that these components are lacking high titre anti-A or anti-B. However Transfusion Service testing for high titre anti-A/B cannot confidently exclude all dangerous donations and the Services should be encouraged to ensure that sufficient group A platelets are always available for these patients.

Action: UK Transfusion Services

7 Delayed Transfusion Reactions

Definition

Delayed transfusion reactions are defined in this report as those occurring more than 24 hours following a transfusion of blood or blood components. In practice, these are usually delayed haemolytic reactions due to the development of red cell alloantibodies. Simple serological reactions (antibody development without a positive DAT or evidence of haemolysis) are excluded.

This category accounted for 6.8% of non-infectious hazards reported and 6.7% of all hazards.

32 new initial reports were received and 2 were brought forward from the previous year. 2 additional reports were received which were not included in the analysis for this chapter. 9 reports received during the reporting period are still awaiting completion of a questionnaire and will be presented next year.

This chapter highlights the main findings from 25 completed questionnaires (23 from the current reporting year).

Age and sex

Age (25 reports)

Age range 31 -83 years

Median age 70 years

Sex (25 reports)

Males 8

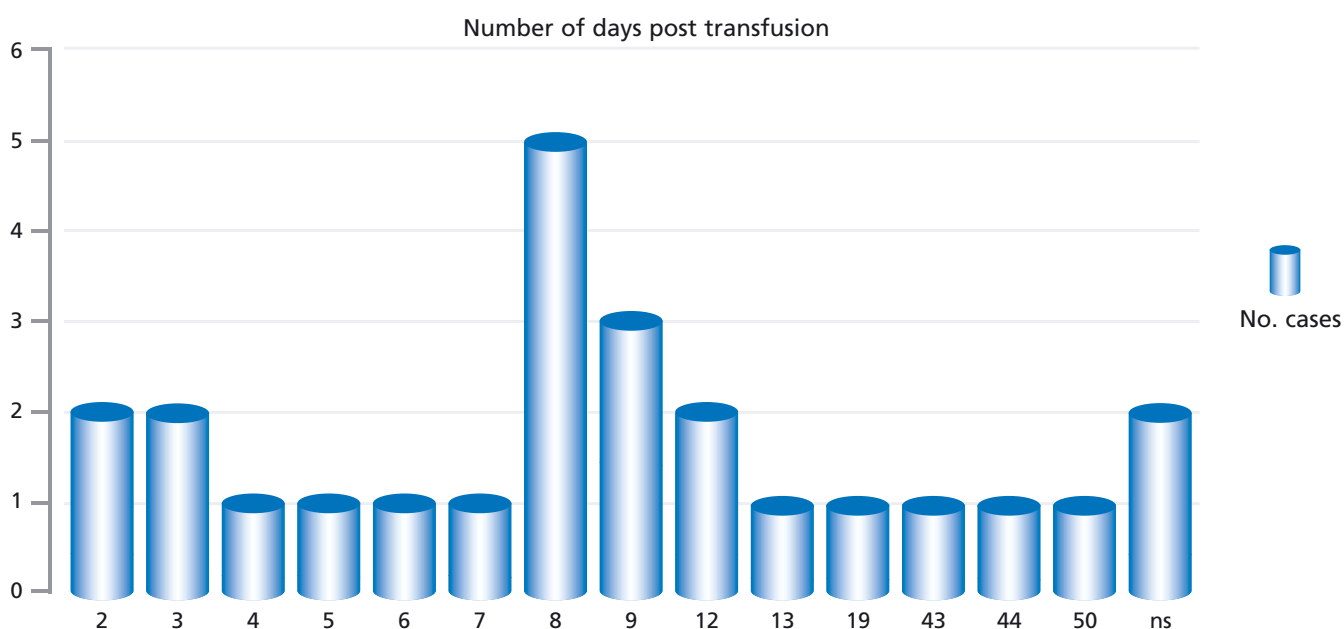
Females 17

Interval between transfusion and symptoms

Figure 8 shows the interval in days between the implicated transfusion and signs or symptoms of a DHTR. The intervals given are necessarily those when the signs or symptoms were first noted. However, it is possible that some extravascular haemolysis was ongoing during or shortly after the transfusion in those cases where the causative antibody was detectable pre-transfusion, or when the reaction was clinically noted within 48 hours of the transfusion.

Figure 8

Interval between transfusion and symptoms



Median = 8 days

Range = 2 to 50 days

Reactions reported

There were 3 deaths in this group; none thought to be related to the transfusion. One patient required ICU admission, but did not suffer any long term morbidity. The remaining patients suffered minor or no morbidity.

All reported reactions were probably caused by the administration of allogeneic red cells. In 2 cases the causative antibody was detected pre-transfusion: in case 3, anti-M present in a mixture of antibodies was not initially detectable at 37°C, but contributed to a severe DHTR 9 days later; in case 21 an unidentified antibody present in a mixture caused a reaction within 2 days of the transfusion. In this latter case it is likely that there was ongoing extravascular haemolysis during or soon after the transfusion was started, and the same patient suffered an immediate haemolytic reaction following a subsequent transfusion (see vignette).

In 3 cases, the causative antibody may have been detectable pre-transfusion, but there is insufficient evidence to be certain. In case 13 (see vignette) one specificity was retrospectively found in the pre-transfusion sample but detectable only with an enzyme technique, and a second enzyme-only antibody was retrospectively detected in a further sample taken 8 days later, and 5 days prior to signs of a DHTR. In the other 2 cases (case 8 and 25), anti-Kidd antibodies were probably present in the pre-transfusion samples, but insufficient testing was undertaken to be certain (see vignettes).

Thirty-nine new antibodies were identified post-transfusion in 23 patients. In addition to the 5 cases already described, 7 had pre-existing antibodies: 6 received appropriately phenotyped blood and the 7th (with anti-Kp^a) received crossmatch compatible blood, but all developed further specificities as a result of the transfusion.

Six cases had no reported history of previous transfusion or pregnancy. In one of these (case 16), the reaction may have been due to primary sensitisation, the antibody being detected 44 days post transfusion (grade 2/3). In the other 5 cases (2 male, 3 female), the antibodies were found within 13 days of the transfusion, and it must therefore be assumed that these patients had received previous transfusions or had previously been pregnant.

Two had a negative DAT: both had clear-cut haemolytic reactions (grade 3) with identifiable red cell antibodies.

Urgency of transfusion requirement

The transfusion was said to be routine in 15 patients and an emergency in 10. However two of the routine transfusions took place between 8pm and midnight, classified as during a shift system, although testing took place during routine hours; in one case the pre-transfusion testing took place between midnight and 8am, classified as on-call, although the transfusion took place during routine hours, and in 1 case both the testing and the transfusion took place between midnight and 8am, classified as on-call.

New post transfusion antibodies

Table 12 shows the specificity of all new antibodies detected post-transfusion and table 13 antibodies in individual patients.

Table 12 – New specificities by blood group system

Antibody specificity by blood group system	Number of cases	Sole <i>new</i> antibody
Kidd		
Jk ^a	10	7
Jk ^b	6	3
Rh		
C ^w	1	0
E	7*	2 (1 with anti-c)
c	3	1 (with anti-E)
e	1	0
Kell		
K	2	0
Kp ^a	1	0
Duffy		
Fy ^a	2	2
MNSs		
S	2	0
Other		
P ⁱ	1	0
Ch	1	0
Kn ^a	1	0
A ₁	1	0

* one retrospectively detected pre-transfusion but by enzyme only

Table 13 New post-transfusion antibodies in individual patients

Case number	New antibody (ies)	Comments
1	Jk ^b +S+C ^w	Pre-existing anti-Fy ^a
2	Jk ^b	Pre-existing anti-K
3	None	Pre-existing anti-Fy ^a + c+E+S+M+Cs ^a . Unit not typed for anti-M as not detectable at 37°C until post transfusion
4	E+Kp ^a + non-spec enzyme antibody	
5	c+E	Known pre-existing anti-K but no identification panel performed pre-Tx
6	Jk ^a	Pre-existing anti-E+K
7	Jk ^a + non-spec enzyme antibody	
8	Jk ^b + P ₁	Known pre-existing anti-E but no identification panel pre-Tx
9	Jk ^a	
10	Jk ^a	
11	c+E+Ch+K	
12	Jk ^a	
13	Jk ^a +K+E	Anti-Jk ^a by enzyme only, post tx. Anti-E and -Jk ^a both detected retrospectively by enz only.
14	Jk ^b	
15	Fy ^a	
16	E+Jk ^a +?auto anti-c	
17	Jk ^b	
18	Jk ^a	Pre-existing anti-D+?C
19	e+A ₁	Pre-existing anti-K
20	Fy ^a	Pre-existing anti-Kp ^a
21	None	Anti-c+E+Jk ^b +Cw+ further unidentified antibody – eventually identified as anti-Do ^a
22	Jk ^b +S+Kn ^a	Positive screen pre-transfusion but ID panel negative
23	E	
24	c+E+Jk ^a +non-spec cold	
25	Jk ^a	Known pre-existing anti-K + cold auto, but no identification panel performed pre-Tx

Severity of reaction/ clinical sequelae

Symptoms and signs could be divided into 4 categories as follows:

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

Group 1

There were 7 patients in this group. One was already on ICU but all 7 survived with no sequelae. One was jaundiced and had a falling Hb, but it is likely that these signs could be attributed to the underlying clinical condition. One had a fever reported during transfusion, but there is no evidence that this was related to the antibody.

Group 2

There were 4 patients in this group. Two were already on ICU, but all 4 in this category survived with no sequelae. Although one of these patients was jaundiced and was reported to have dark urine (case 19), these findings could also be explained by the underlying clinical condition.

Group 3

There were 11 patients in this group, of whom 7 survived with only short term symptoms and no risk to life, although 2 did require admission to the ward (cases 1 and 16). One of these (case 16) who gave no previous history of transfusion was re-admitted after 44 days, with an Hb of 44g/L, a raised bilirubin and no evidence of any remaining transfused cells; the picture was complicated by his history of bleeds due to alcoholism.

Two patients died, with the cause unrelated to the transfusion.

One patient with sickle cell disease (case 3 – see vignette), suffered a life-threatening drop in Hb to 25g/L, but survived with no long term ill effects. One patient required ICU admission (case 22) but also survived with no long term ill effects.

Group 4

There were 3 patients in this group. One was already on ICU and died as the result of a ruptured abdominal aortic aneurysm. One (case 11) had to be re-admitted with haemoglobinuria. The third survived with no long term ill effects.

Table 14

Individual new antibodies grouped by severity of signs and symptoms

Group 1		Group 2		Group 3				Group 4	
Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity
4	E+Kp ^a	15	Fy ^a	1	Jk ^b +S+C ^w	18	Jk ^a	11	c+E+K+Ch
7	Jk ^a	17	Jk ^b	2	Jk ^b	21	None	14	Jk ^b
8	Non specific +E+Jk ^b +P ₁	6	Jk ^a	3	None	22	Jk ^b +S+Kn ^a	20	Fy ^a
9	Jk ^a	19	e+A ₁	5	c+E	24	c+E+Jk ^a +no n-spec cold		
12	Jk ^a			10	Jk ^a				
23	E			13	Jk ^a +K+E				
25	Jk ^a			16	E+Jk ^a + ?auto anti-c				

Analysis of serological information

Table 15 gives information on the techniques used for antibody screening in the 25 reported cases. An IAT crossmatch was performed in 18 cases (including all those where the antibody screen was positive), an immediate spin crossmatch in 1 case, and electronic issue in 6 cases.

Table 15

Techniques used for antibody screening and crossmatching

IAT screening technology	Number of cases
CAT	23
NISS tube	1
Unknown to reporter*	1

* Performed by the Blood Centre

IAT Technology

Excluding the case where pre-transfusion testing was performed at the reference centre, 96% of cases were performed using Column Agglutination Technology (CAT). This reflects current practice in the UK where approximately 82% of antibody screens in non-reference laboratories are performed using CAT (data from UK National External Quality Assessment Scheme (UK NEQAS) questionnaire, February 2003).

Automation

At least 83% of the CAT users utilised automation (no data was available in 2 cases). In 2002, only 43% of UK laboratories utilised automation for antibody screening (data from UK NEQAS questionnaire, July 2002). The significance of this finding is as yet unknown, given the small number of cases.

Plasma/serum

Plasma was used in 22 cases (92%) and serum in 2 cases (1 not stated). This probably reflects current practice with data obtained from a UK NEQAS questionnaire (Feb 2003) showing that approximately 86% of antibody screens undertaken in UK hospitals are performed using plasma rather than serum.

Screening cells

In eighteen cases the screening cells bore apparent homozygous expression of the relevant antigen. In 6 cases, although not stated, it is probable that they did, and in the last case no information was available as the pre-transfusion testing took place at a different site.

The majority of reporting laboratories utilising a CAT technique, used screening cells that were validated for use by the supplier. Of the 5 that used alternative screening cells, only 2 stated that they had validated the cell suspension in-house prior to use. There was no information available from 4 reporting laboratories.

Incubation time and details of techniques

Incubation times for antibody screening/identification and crossmatching by CAT varied from 10 to 30 minutes, but all were within recommended limits. All cell:serum ratios were correct for the column technology used and manufacturer's instructions were followed in all cases where information is available (21 of 23 cases). The serum:cell ratio used in the NISS tube case was 2:1; this is lower than the recommended 4:1¹⁸ (case 25 – see vignette).

Retrospective testing

In only 6 (25%) cases was the pre-transfusion sample retested, and the same result was obtained in 5 (83%) of them. In all 6 cases a different individual repeated the testing, but in the 5 cases where the same result was obtained, the same techniques were used as for pre-transfusion testing. In the sixth case an enzyme technique was included in the retrospective testing and enzyme only antibodies were detected, one of which became reactive by IAT post transfusion (see vignette). In these 6 cases the DTR was not recognised until 6-12 days post transfusion. In 4 cases where retrospective testing was not performed, the DTR was reported to have occurred 2-4 days post transfusion and samples for crossmatching were taken within 48 hours of the transfusion.

Direct Antiglobulin Test

The post transfusion DAT was reported to be negative in 2 cases. In 8 cases the coating was IgG only, in 2 cases C3d only and in 9 cases both (in addition, one had IgM coating).

Interval between drawing the crossmatch sample and transfusion

Table 16

Interval between drawing the crossmatch sample and transfusion

Interval between sampling and transfusion	No. cases
<48 hours	22
5 days	1
6 days	1

As far as it is possible to tell from the questionnaires, all of the samples were taken within the time limits recommended in the BCSH guidelines.¹⁹

Reporting to Blood Centres and Hospital Transfusion Committees

A total of 15/24 (63%) incidents were reported to the local Blood Centre and 21/24 (88%) to the HTC. No data was available for the remaining case. There seems to be a gradual upward trend in reporting cases of DTR to the local Blood Centre (46%, 49% and 58% for the previous 3 years), whereas reporting to the HTC is more frequent but more erratic (79%, 85% and 73% for the previous 3 years).

Case histories of some of the more informative or unusual cases are given below:

Case 3

A 37 year old female patient with sickle cell disease received an 8-unit emergency exchange transfusion following a stroke. The patient was known to have anti-Fy^a+c+E+S+M+Cs^a and crossmatched antigen negative blood was provided for all except the anti-M, which at the time was not detectable at 37°C and was therefore thought to be of no clinical significance. Six days later she received a 3 unit top-up transfusion, crossmatched against a fresh sample, and again antigen negative for all except the anti-M. Two days later she had dropped her Hb to 25g/L, the DAT was positive and anti-M was identified both in the plasma at 37°C and in an eluate made from the patient's red cells (tested by IAT). A further 3 units of M- blood were transfused and produced a short-lived increase in Hb. The short-lived increase in Hb combined with an increase in the level of HbS% and no reticulocytopenia, suggests destruction of both transfused cells and patient's own cells. The haemolysis was therefore likely to be the result of a combination of DHTR due to anti-M, and hyperhaemolysis (of patient's own and transfused cells).²⁰

Case 13

An 83 male patient with MDS received a 2-unit top up transfusion on day 1; the antibody screen was negative. On day 9, a new sample was taken; again, the screen was negative and a further 2 units were crossmatched and transfused. On day 12, a new sample showed a weakly positive antibody screen by IAT, but the specificity was not clear; however anti-E and anti-Jk^a were revealed by a 2-stage enzyme technique and the DAT was weakly positive. On day 13, a further sample was taken, and anti-E and anti-K were identifiable by IAT; anti-Jk^a was still only detectable by 2-stage enzyme. The patient's Hb fell from 96g/L to 80g/L between day 10 and day 16, the bilirubin rose from normal levels to 53µmol/L by day 16 and spherocytes were noted on the blood film. A new sample, taken on day 16 and plasma aliquots from previous samples were referred to the NBS

reference laboratory. They confirmed anti-E+K by IAT and enzyme-only anti-Jk^a in the day 16 sample, enzyme-only anti-E and anti-Jk^a in the day 9 sample, and enzyme-only anti-E in the day 1 sample. One of the units transfused on day 1 was Jk(a+) and the other K+; one of the units transfused on day 9 was E+. It is not clear which of these antibodies contributed to the DHTR.

Case 21 (and case 3 from the ATR section)

A 68 year old female patient with myelodysplastic syndrome required a 2-unit top-up transfusion. The patient was known to have anti-c+E+Jk^b+C^w, but further reactions by IAT could not be identified, even by the reference centre. It was suspected that the unidentified antibody was HLA related, and R₁R₁ Jk(b-) red cells, weakly incompatible by IAT, were issued as suitable for transfusion. Two days later the patient had chills, fever, jaundice and a falling Hb, and the DAT (not performed pre-transfusion) was positive with anti-IgG. The patient had a further red cell transfusion three weeks later with weakly incompatible R₁R₁ Jk(b-) cells, which were selected and crossmatched by the Reference Laboratory, using an IAT and one stage papain technique; at this stage the antibody was suspected to be a 'high-titre, low-avidity' (HTLA) specificity (within the Knops blood group system). However, she became restless, and developed a fever, chills and hypotension during the transfusion, which was continued at a slower rate. The International Blood Group Reference Laboratory confirmed the presence of an anti-Do^a in the post-transfusion sample four weeks later.

The frequency of Do^a is 66% in northern European donors; therefore Do(a-) blood is not difficult to find. However, Dombrock antibodies are difficult to identify and usually occur in mixtures of antibodies. For this reason, their presence should be considered when unidentifiable reactions occur in the presence of other red cell alloantibodies.

Case 5

A 31 year old female patient with anaemia due to Crohn's disease was routinely transfused as an outpatient with 3 units of red cells. She was known to have anti-K, last investigated 6 weeks previously and as there was no history of transfusion, an identification panel was not performed (in line with laboratory policy). The patient reported verbally that she had anti-E. The blood was K-, E- and crossmatch compatible. Eight days later the patient presented with dark urine and jaundice; the DAT was positive and anti-c+E+K was identified in her plasma. A retrospective panel on the pre-transfusion sample confirmed that only anti-K was detectable (by both IAT and enzyme techniques). A subsequent enquiry from a neighbouring hospital revealed detection of enzyme only anti-c+E in 1994.

Two similar cases are described where pretransfusion testing did not include antibody identification, despite known existing antibodies.

Case 8

A 35 year old male patient with alcoholic liver disease and bleeding varices required an emergency transfusion of several different blood components. The patient had a known anti-E and E negative units were crossmatched by a manual DiaMed technique and issued as compatible without an identification panel. Two days after transfusion, a further sample revealed non-specific reactions by IAT in addition to the anti-E; the DAT was positive with IgG, IgM and C3d reagents (not tested pre-transfusion). No retrospective testing was undertaken on the pre-transfusion sample as it was no longer available. The Blood Service reference laboratory identified anti- E+Jk^b+P₁. The patient had raised levels of plasma bilirubin and alanine aminotransferase (ALT), and the Hb fell, all of which were consistent with his clinical condition. It is therefore not clear whether or not the patient suffered from a haemolytic transfusion reaction, and the case has been classified as a category 1.

Case 25

Two units of blood were requested for a 71 year old female patient on-call for a non-urgent top-up transfusion, the reason for the anaemia not being recorded. The patient had been transfused 9 weeks earlier, when pre-transfusion testing revealed anti-K and a non-specific cold autoantibody, confirmed by a reference centre. The on-call BMS screened the plasma and crossmatched the units using a normal ionic-strength saline (NISS) tube technique (2:1 serum to 3% cell ratio), rather than their routine automated BioVue technique, because the presence of the cold antibody interfered with the reactions obtained using BioVue. However, they did not use an antibody identification panel. The two units were compatible and transfused and a third unit was requested. The reactions to the third unit were recorded as 'sticky', but this was assumed to have been caused by the cold antibody and the unit was transfused. The patient spiked a temperature during the transfusion of this 3rd unit, but no investigations were undertaken. Approximately 3 days later, a junior house officer queried the febrile episode as a transfusion reaction and another sample was taken and sent to the reference laboratory for investigation. Anti-Jk^a was identified (in addition to anti-K and a non-specific cold antibody) in both the plasma and in an eluate made from the patient's cells. The pretransfusion sample was still available, and antibody screening and crossmatching results gave the same reactions as they had done during pretransfusion testing. An identification panel was still not performed. The Jk^a antigen status of the transfused units was not recorded.

These two cases were difficult to categorise, since it is likely that the Kidd antibodies would have been detectable pre-transfusion, had the appropriate tests been performed. Had this been the case they would have been categorised as IBCT. In addition, there is no strong evidence of haemolysis in either case, which makes them serological rather than haemolytic transfusion reactions. Furthermore, the latter case was only detected because of belated investigation of a febrile reaction during transfusion and isolated febrile reactions are not reportable to SHOT.

BCSH guidelines¹⁹ recommend that an identification panel be performed every time a new sample from a patient with a positive antibody screen is tested. The pre-transfusion sample was only kept for a very short time in case 8 (probably less than 3 days), and in case 25, although still available, was not fully retested. It is particularly surprising that an identification panel was not performed in case 25, since the patient had been recently transfused, the crossmatch was weakly incompatible and the patient suffered a febrile reaction during the transfusion. BCSH guidelines¹⁸ also recommend a serum:cell ratio of 4:1 for a NISS tube technique to obtain maximum sensitivity.

COMMENTARY

- Kidd and/or c antibodies accounted for approximately 72% of all new antibodies, and were implicated in 83% of all patients in whom antibodies were found.
- 67% of patients developed more than one antibody. This highlights the importance of a thorough antibody investigation in patients who have already developed a red cell antibody as they are likely to be good responders.
- There were 3 cases (5, 8 and 25) where the patient had a known antibody, but an antibody identification panel was not performed prior to transfusion,; in one of these cases there was a history of recent transfusion. This reflects non-compliance with BCSH guidelines,¹⁹ which state "If the patient is known to have a red cell alloantibody, the serum/plasma should be checked on each occasion of testing to exclude the development of further alloantibodies".
- There is no evidence that laboratories are not following guidelines with respect to timing of samples in relation to the transfusion.
- Retrospective testing of the pre-transfusion sample was only undertaken in 25% of cases. There is a suggestion that some laboratories are discarding the samples very soon after transfusion.
- It would appear that some laboratories are using screening cells that have not been validated for the IAT technology used. Data from UK NEQAS and the Welsh Assessment of Serological Proficiency Scheme (WASPS) exercises (99E7/00R9 and W10/03, respectively) has shown that a cell suspension lower than that recommended by the manufacturer can result in weak antibodies being missed.

RECOMMENDATIONS

- Investigation of a suspected DHTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. This may involve referral to a reference centre.

Action: Hospital blood transfusion laboratories

- Automated systems or changes to IAT technology should be validated using a range of weak antibodies to ensure appropriate sensitivity.

Action: Hospital blood transfusion laboratories

- Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies. 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.¹⁹ 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

8 Transfusion Related Acute Lung Injury

Definition

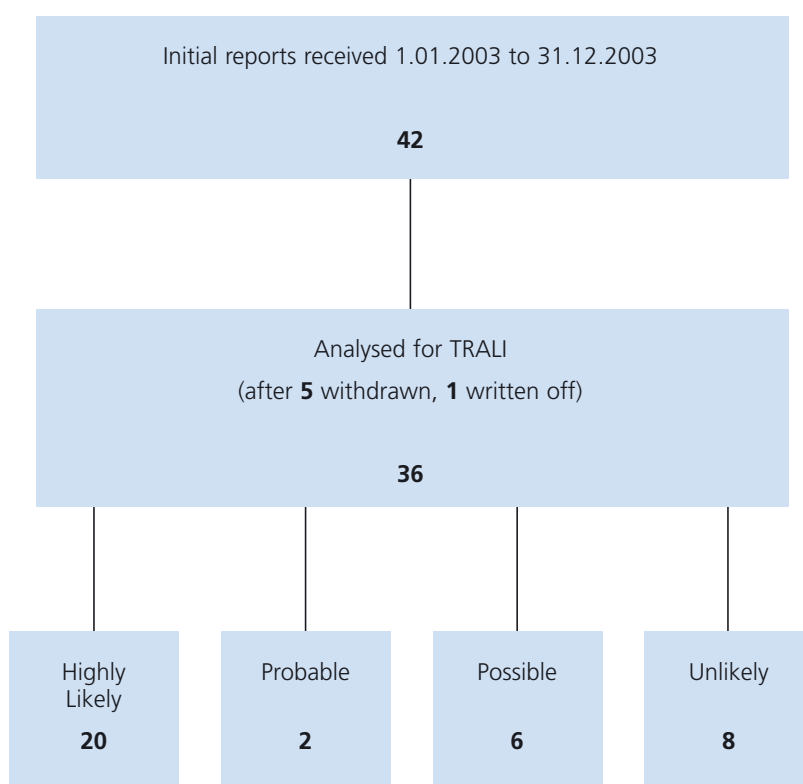
Transfusion-related acute lung injury was defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates occurring during or in the 24 hours after transfusion, with no other apparent cause.

Forty-two case reports of suspected TRALI were received in this reporting year. Of these, 5 were subsequently withdrawn by the reporters for a variety of reasons. This represents an increase in the number of reports compared with previous years. In the 12 months period from 01/10/2001 to 30/09/2002 there were 26 new reports of suspected TRALI and 15 new reports in the corresponding period from 2000 to 2001.

Thirty-six cases were analysed. Of these, nine patients died, 22 suffered short term major morbidity and five suffered minor morbidity. Of the nine patients who died, the reporters considered death to be definitely due to transfusion in one case, possibly due to transfusion in seven cases and unrelated in one case. Of the 27 patients who survived, outcomes were good with only one patient recorded as having longer term morbidity. This patient was highly likely to have had TRALI. A summary of cases is shown in Figure 9.

Figure 9

Summary of cases reported



Assessment of TRALI reports

TRALI can be a difficult diagnosis to make as symptoms and signs may be indistinguishable from other causes of acute lung injury and there is no single test for this condition. A high index of suspicion is required at the time and serological investigation of donors and patients after the event. If the symptoms and signs occur 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).

Results of antibody investigations may not be definitive. Because of the frequency of leucocyte antibodies in the donor population, donor antibodies would also be found in uneventful transfusions if they were similarly investigated. In a recent NBS study of 1166 female donors HLA antibodies were found in 14.5% (personal communication, Dr S. MacLennan). The likelihood of a case being TRALI was assessed by two medical specialists from the SHOT team (one a consultant in anaesthesia and critical care, the other a consultant in transfusion medicine/immunology). Reports were graded on the basis of clinical features and available laboratory results. Complete results of relevant serological investigation were not available in six cases.

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.

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
TRALI Table 2	Treatment, investigation results and likelihood of case being TRALI
TRALI Table 3	Clinical and radiological features of cases reported as TRALI

Patient characteristics

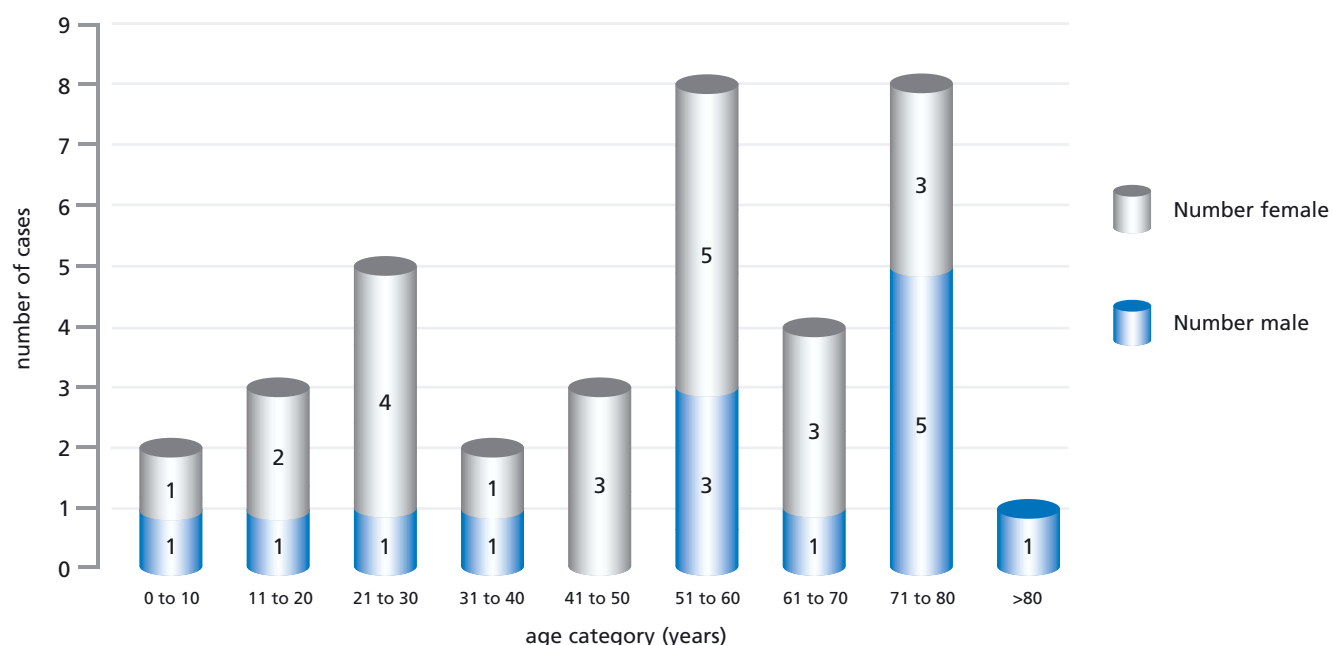
Details of all reported cases are tabulated in **TRALI Table 1** on the SHOT website.

Age and sex

An analysis of cases by age and sex is shown in Figure 10. Cases of TRALI were reported in all age groups. More patients were female (22) than male (14). Analysis of 145 TRALI cases reported by SHOT from 1996 to the present shows only a slight excess in females (77 cases, 53%) compared with males (68 cases, 47%).

Figure 10

TRALI cases by age and sex



Reason for transfusion

Reports have been analysed according to the reason for transfusion (Figure 11). The most frequent underlying reason for transfusion was haematological disease (15 cases, 42 %); surgical procedures accounted for 10 (28%) cases. Medical and obstetrics and gynaecology specialities contributed five and four cases respectively. Two reports concerned the use of FFP for warfarin reversal; details of clotting investigations and whether the patients were bleeding were not provided in these reports. There is insufficient clinical information reported to allow accurate assessment of the appropriateness of the above transfusions.

Figure 11

TRALI cases by indication for transfusion



Clinical features

Clinical presentation

Details of all reported cases are tabulated in **TRALI Table 2** on the SHOT website.

All suspected cases were reported to have been hypoxic and 28 of 36 (78%) patients were treated in Intensive Care Units. Twenty two patients required assisted ventilation. The clinical descriptions of reactions suspected to be TRALI were very similar for patients in whom the diagnosis was subsequently supported by serological results and for those without such supporting evidence. Fever was reported in 13 of 35 patients, in whom this was recorded, with similar numbers in the group with serological support (7 of 21, 33%) and in the group without this evidence (6 of 14, 43%) (Chi-Square, $p=0.568$). Hypotension was reported as part of the reaction in 23 cases. This feature was reported significantly more frequently in patients with supporting serological evidence (17 of 21, 81%) than in those without (6 of 15, 40%) (Chi Square, $p=0.012$). Reporting of the presence or absence of heart failure was incomplete (10 reports) but there were six reports of clinical features suggesting heart failure including two who had subsequent serological support for a diagnosis of TRALI.

Patient outcomes

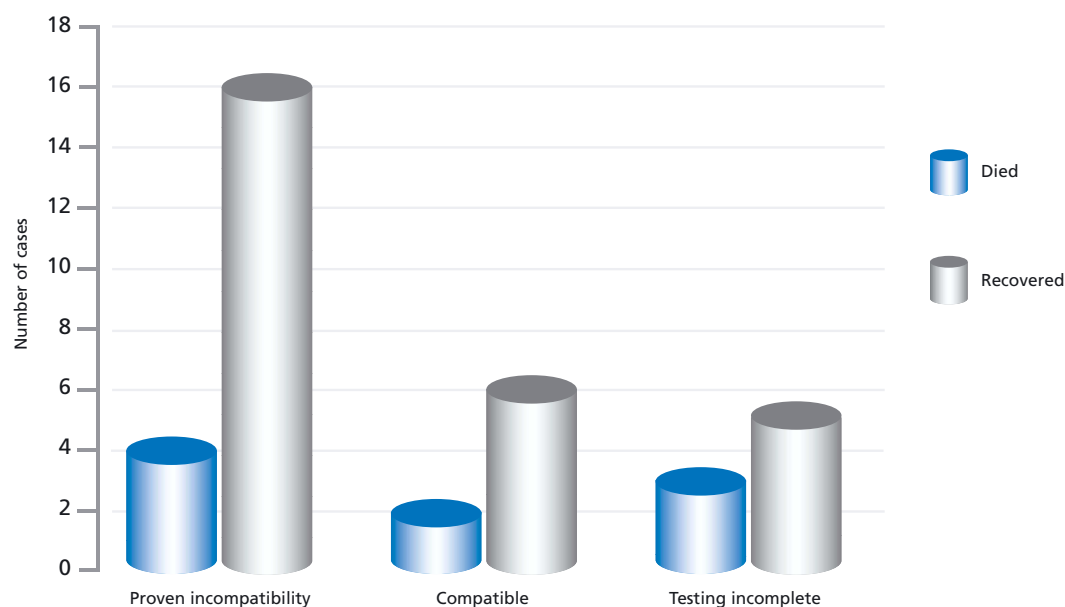
Details of all reported cases are tabulated in **TRALI Table 3** on the SHOT website.

Nine patients died but the majority of patients (26) made a full recovery. One patient was reported to have recovered but with persisting unspecified morbidity. Of those patients who died, the reporters considered death to be 'definitely due to transfusion' in one case, 'possibly due to transfusion' in seven cases and 'unrelated to transfusion' in one case. In two of the cases where the reporter considered that death was 'possibly due to transfusion' heart failure was present and investigation of all relevant donors in these two cases was negative for leucocyte antibodies.

Patient outcomes (death or recovery) have been analysed according to the results of serological investigations. Results were grouped according to whether leucocyte incompatibility was present, absent or not completely tested and are shown in Figure 12. Of the nine deaths: four were in cases with proven leucocyte incompatibility; incompatibility was excluded in two and the clinical picture was not typical; non-specific leucocyte antibodies were found in two but follow-up samples for crossmatch were not available and in one case tests are still in progress. Incomplete results are more likely in those who have died because stored patient samples are unsuitable for leucocyte crossmatch but may be suitable for typing.

Figure 12

Patient outcomes analysed by leucocyte compatibility



The overall survival in all cases was 75% and in the subgroup of 21 cases with proven leucocyte incompatibility survival was 81%. The single case of persisting unspecified morbidity had proven leucocyte incompatibility.

Donors

All donors in whom relevant antibodies were identified were female. In general, untransfused males were excluded from investigation. Transfused males were investigated but none was identified with relevant antibodies.

Laboratory results

Details of all reported cases are tabulated in **Table 2** on the SHOT website.

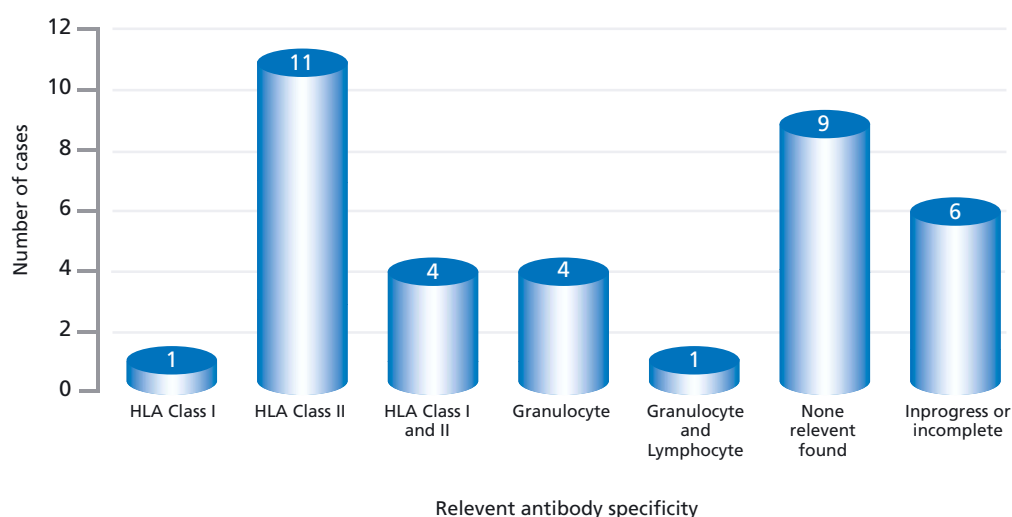
Each case was referred to the local Blood Centre for investigation and in all cases relevant donor and patient samples were investigated at Reference Laboratories.

Donor antibodies

Relevant donor leucocyte antibodies were found during investigation of 21 of 36 cases. These were either specific antibodies (18 cases) corresponding with identified patient lymphocyte and/or granulocyte antigens or leucocyte antibodies without an identified specificity but with positive donor/patient crossmatch results (three cases). Analysis of the results of investigation for donor white cell antibodies is shown in Figure 13. Relevant HLA antibodies were identified in 16 cases. Of these, HLA Class I antibody alone was identified in one case;

HLA Class II antibodies were implicated either alone or in combination with HLA Class I in 15 cases. Granulocyte specific antibodies were found less frequently (five cases). Of the remaining 15 cases, nine investigations gave negative results, two investigations revealed antibody but it was not possible to identify whether this corresponded with patient antigen and four investigations are still in progress.

Figure 13 Analysis of results of donor antibody investigations



Patient antibodies

Leucocyte antibodies were found in five patients. In four of these cases, donor leucocyte antibodies were also found which corresponded with patient antigen. In one case, non specific leucocyte antibodies (HLA and granulocyte) were found in the patient and a non specific leucocyte antibody was found in one donor which was negative on crossmatch with patient leucocytes. A crossmatch between patient serum and donor cells was not performed. In no case of TRALI was a patient antibody identified as causative.

Components

Details of all implicated components are tabulated in **TRALI Table 1** on the SHOT website.

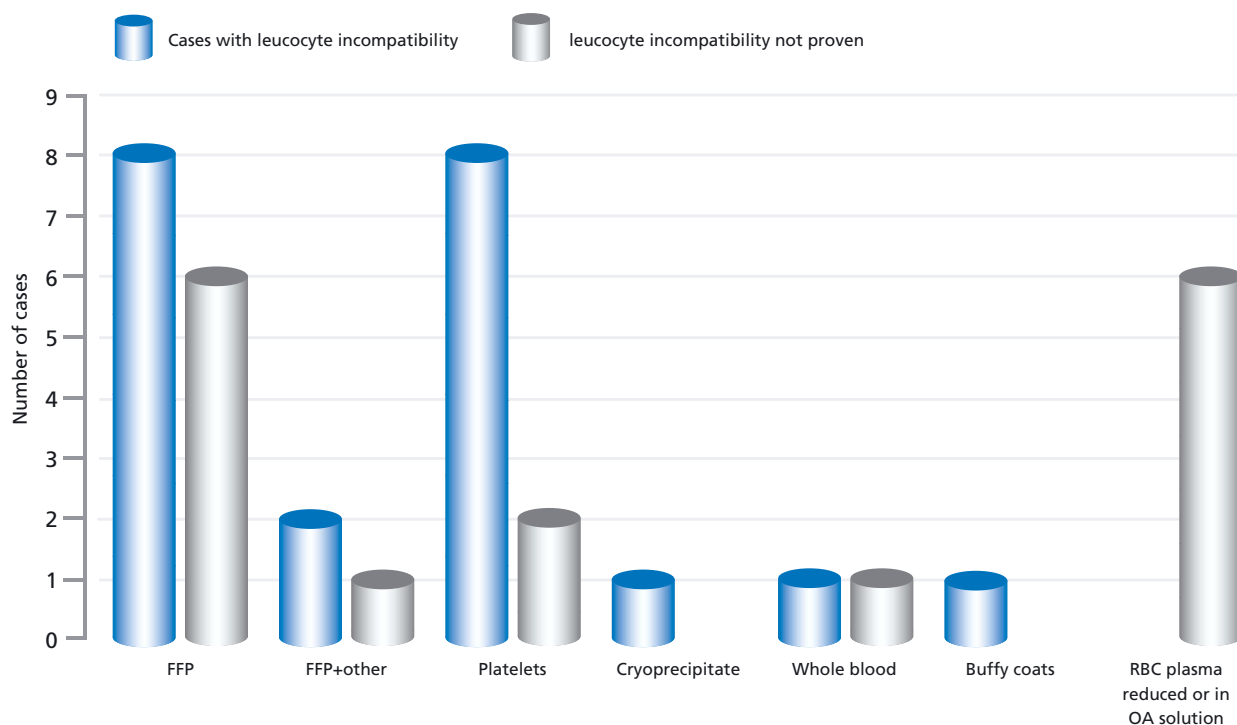
The component most commonly implicated in 36 suspected cases of TRALI was FFP (14 cases) with three additional cases in which a combination of components including FFP was implicated (one implicated case per 27,000 FFP units issued). Platelets were implicated in 10 cases (one implicated case per 25,000 platelet units issued), red cells not identified as whole blood in five cases (one implicated case per 529,000 red cell units issued), whole blood in two cases, a buffy coat in one case and cryoprecipitate in one case. Figure 14 shows an analysis of implicated components. Cases have been divided into two groups: one includes 21 cases in which there was proven donor/recipient leucocyte incompatibility and the other comprises 15 'other' cases in which incompatibility was not tested or not detected. All except one case in the subgroup with proven leucocyte incompatibility were assessed as 'highly likely' to be TRALI, the remaining case had multiple risk factors for ARDS and was classified as 'probable'. It is notable that implicated components received by this subgroup with proven leucocyte incompatibility were FFP, platelets, whole blood, buffy coat and combinations including FFP. All of these components are plasma rich apart from the buffy coat which would have contained approximately 30mL plasma.

Whole blood was the implicated component in two reports; one of these was confirmed by serology, the other was not but the clinical picture was very suggestive of TRALI. Both cases were adults, one was a man aged 52 who had a gastrointestinal haemorrhage and was transfused with four units of whole blood, the other case was a 27 year old woman who was transfused with four units of whole blood to treat post partum anaemia. Both patients recovered fully following intensive care including ventilation. Whole blood is infrequently issued to hospitals compared with other red cell components (red cells in optimal additive solution and plasma reduced red cells). In 2003, 0.035% red blood cells were issued as whole blood from the NBS.

None of the five suspected cases of TRALI associated with red cells not identified as whole blood was confirmed by serological investigation. In this group, one patient was transfused with red cells in optimal additive, three patients received red cells of unreported type and one received plasma reduced red cells. Information regarding the type of red cell component was not requested on the SHOT TRALI questionnaire.

Figure 14

Components implicated in TRALI



Case histories

The case numbers used here correspond with those used on the web based tables.

Case 5

A 78 year old man underwent a planned repair of an abdominal aortic aneurysm. He had a history of hypertension and had mild renal impairment. During surgery he had an episode of myocardial ischaemia, a transient drop in oxygen saturation when the circulation was restored to the legs and prolonged bleeding. Post operatively he was admitted to the ICU and remained on a ventilator. At this time he had mild pulmonary oedema. He was then given three units of FFP because of his postoperative bleeding and prolonged prothrombin time. During the third unit of FFP his oxygen saturation dropped suddenly with severe worsening of his pulmonary oedema. He also became febrile and hypotensive. The differential diagnosis at this time was reperfusion injury or myocardial infarction. Central venous pressure was low and echo did not indicate left ventricular dysfunction or fluid overload and myocardial infarction was subsequently excluded. TRALI was later included in the differential diagnosis because of the combination of severe pulmonary oedema, low circulating blood volume and the temporal relationship between the FFP transfusion and his deterioration. He remained on a ventilator requiring intensive support for multiorgan failure until he died eight days post-operatively. The Consultant in Anaesthesia and Intensive Care considered that death occurred as a result of multi-organ failure resulting from severe pulmonary oedema. Serological investigations for TRALI revealed that one donor had HLA Class II antibodies with specificity for HLA DR4 and DQ8. The patient was positive for both antigens and it was concluded that this case was highly likely to be TRALI. The reporter of this case considered that death was possibly due to transfusion but another cause could not be excluded.

Case 6

A 56 year old man underwent splenectomy for refractory immune thrombocytopenia purpura. Pre-operatively, he was otherwise well and was transfused with a unit of pooled platelets as prophylaxis against bleeding. Respiratory problems became apparent post-operatively in the recovery room. Following extubation he developed hypoxia and hypercapnia necessitating reintubation. Bilateral alveolar opacification was seen on chest X ray. He was admitted to the intensive care unit and was ventilated for four days. No evidence of cardiac dysfunction was found clinically or on echocardiography. He recovered without long term morbidity.

Serological investigation revealed anti human neutrophil antigen (HNA) 1a (a granulocyte specific antibody) in a sample from the female donor who had contributed the plasma to the implicated platelet pool. The patient was found to be positive for HNA1a. which provided serological support for a diagnosis of TRALI and the case was assessed as highly likely to be TRALI. The patient also had HLA antibodies that were thought unlikely to be significant. Currently, all blood components are leucodepleted and it is unlikely that the number of residual leucocytes would be sufficient to cause TRALI mediated by leucocyte antibody of patient origin.

COMMENTARY

- TRALI remains a serious consequence of transfusion. There was one patient whose death was considered by the reporter to be 'definitely due to transfusion' and in seven cases death was considered 'possibly due to transfusion'.
- The number of cases reported this year has increased again compared with previous years. It is not possible to determine if this is due to increased awareness of the condition or a true increase in case numbers.
- The cases illustrate that diagnosis of TRALI can be difficult. It is important to investigate suspected cases by referring them to the Blood Service laboratories. Serology is helpful but about 14.5% of female donors will have leucocyte antibodies and their presence in an implicated donor does not necessarily mean that they were interactive with the patient. Full laboratory investigation should include donor/patient leucocyte 'crossmatch' if multi-specific HLA or granulocyte specific donor antibodies are found.
- Analysis of cases shows a preponderance of reports concerning patients with underlying haematological disease. Possible reasons to explain this might include a high awareness of TRALI amongst haematologists; the use of platelets in the treatment of haematological disease; it is also possible that some haematological diseases or treatments might predispose to this condition.
- Plasma rich components were implicated in 20 of 21 cases with proven leucocyte incompatibility between donor and patient.
- The only case of TRALI, confirmed by serology, in which the implicated component was red cells alone involved whole blood. Currently, information on the type of red cell component transfused is not routinely requested by SHOT. In future, it would be useful for SHOT to request and analyse the type of red cell components transfused (whole blood, plasma reduced or optimal additive) in cases of suspected TRALI.
- Following previous SHOT recommendations regarding investigation of TRALI, it is encouraging that in all cases there had been liaison between hospitals and Blood Centres facilitating relevant investigations at reference laboratories.
- Donor HLA Class II antibodies were frequently implicated in cases of TRALI. They were detected in 15 of 21 cases of proven leucocyte incompatibility between donor and patient.
- Similar clinical features were observed in patients who had subsequent serological support for a diagnosis of TRALI and in those who did not. Hypotension was found more often in those with serological support for the diagnosis than in those without.
- A case of TRALI with serological supporting evidence occurred in a patient being treated for thrombotic thrombocytopenia purpura. This had not been seen in previous SHOT reports.
- The UK Transfusion Services introduced a new donor exclusion in April 2004 which relates to vCJD. This applies to blood donors and new apheresis donors who have been transfused since 1980. It is likely that this may reduce the risk of TRALI.
- A recent Consensus Conference on TRALI was held in March/April 2004 in Canada but the final Consensus Statement has not yet been issued. Recommendations from this conference should be considered in future policy making. Any agreed change in the definition of TRALI resulting from this conference will be adopted by the SHOT reporting scheme.
- The NBS has a current TRALI risk reduction project. The first action resulting from this work has been to make FFP from male donors only. Ninety percent success has been achieved with this initiative to date. All FFP imported for children born after January 1st 1996 will also be from male donors. Several years of SHOT monitoring will be needed to assess the impact of such policies.

RECOMMENDATIONS

- Every effort must be made to avoid unnecessary transfusion of plasma rich blood components including FFP and platelets.

Action: Clinicians administering blood transfusion

- FFP continues to be associated with risks of reactions including TRALI and should only be used when clinically indicated in accordance with BCSH guidelines.¹² Guidelines for the management of high INRs due to warfarin therapy should also be followed.¹³

Action: Clinicians administering blood transfusion

- Transfusion of whole blood should be discouraged.

Action: HTTs

- Hospital staff should continue to be aware of TRALI and report possible cases to the local Blood Centre to facilitate investigation. Continued education of all relevant staff about this condition is encouraged.

Action: HTTs; clinicians administering blood transfusion

- Cases should be evaluated early by the consultant(s) involved and there should be early liaison with the local Blood Centre. A team approach including the haematologist and chest physician and/or ICU consultant will definitely be helpful.

Action: Clinicians administering blood transfusion plus haematologists, chest physicians and ICU consultants

- Serological investigation of suspected TRALI cases must include tests for antibodies to HLA Class II, HLA Class I and granulocyte specific antigens.

Action: UK Transfusion Services

- The NBS TRALI risk reduction project has led to the implementation of procedural changes such as using plasma from male donors only for FFP. UK Transfusion Services should continue with implementation of such initiatives; attention is also being paid to the plasma contribution to platelet pools and reducing the risk of TRALI posed by female apheresis donors.

Action: UK Transfusion Services

9 Post-Transfusion Purpura

Definition

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

Two cases were reported as possible PTP. One of these did not fulfil the definition for PTP and has been excluded. Details of the confirmed case are provided below.

Case history

A 65 year old female with chronic obstructive pulmonary disease developed pneumonia resulting in respiratory arrest following which she required ventilation. *Clostridium difficile* gastroenteritis and methicillin resistant *staphylococcus aureus* septicaemia complicated her illness. She developed disseminated intravascular coagulation with a Hb of 86 g/L and platelet count of $16 \times 10^9/L$ following which she was transfused uneventfully with two units of apheresis platelets and five units of red cells. Her platelet count recovered to $327 \times 10^9/L$. She developed further thrombocytopenia ten days after her transfusions with purpura and minor haemorrhage. Her platelet count dropped to less than $10 \times 10^9/L$. She was treated with intravenous immunoglobulin 25g /day and steroids. Her platelet count recovered to $> 50 \times 10^9/L$ in 13 days and to greater than $150 \times 10^9/L$ in 15 days. She made a full recovery, which was maintained after steroid withdrawal over five to six weeks

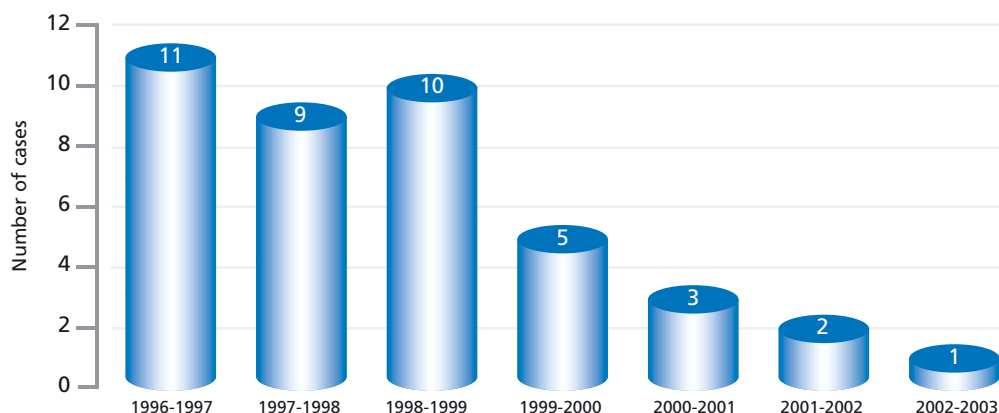
Investigation revealed anti HPA 1a and anti HLA antibodies. Her platelet genotype was HPA1a negative. These results are consistent with a diagnosis of PTP due to anti HPA 1a. She had had three pregnancies and no history of neonatal alloimmune thrombocytopenia in any baby. The interval between her most recent pregnancy and the implicated transfusion was more than 20 years. She had also been transfused previously, less than one year before the implicated transfusion. This was not complicated by any form of transfusion reaction.

Cumulative data on PTP

Figure 15 shows the number of cases of confirmed PTP reported to SHOT each year since 1996. This graph differs from a similar graph in the last SHOT report because 5 suspected but unconfirmed cases of PTP from previous years have been excluded from analysis this year.

Figure 15

Number of cases of confirmed PTP reported to SHOT each year



COMMENTARY

- A single case of confirmed PTP was reported this year. The drop in numbers of suspected cases of PTP since the introduction of universal leucodepletion in 1998 has been maintained.
- The case reported above was female; this is consistent with previous years. Overall, including this year, there have been 41 cases of confirmed PTP reported since 1996. Of these, 40 were female and one was male. A history of previous pregnancy was reported in each female case. The male patient had a history of previous transfusion before the implicated transfusion.
- The only relevant antibody identified this year was anti HPA 1a. This has been the most commonly implicated platelet antibody; it was identified in 34 of 41 (83%) cases of antibody-proven PTP reported to SHOT since 1996.

RECOMMENDATIONS

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

10 Transfusion-Associated Graft-Versus-Host Disease

Definition

Transfusion-associated graft-versus-host disease was defined as the development of the classical symptoms of fever, rash, liver dysfunction, diarrhoea and pancytopenia occurring 1-6 weeks following transfusion, without other apparent cause. The diagnosis was usually supported by skin/bone marrow biopsy appearances and/or the presence of circulating donor lymphocytes.

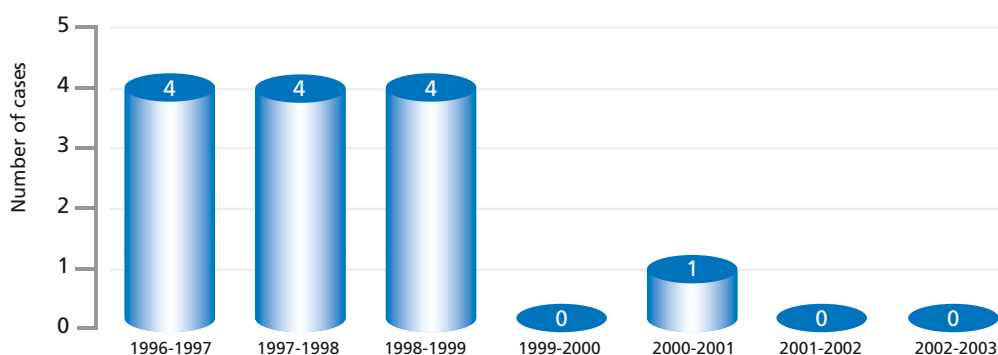
There were no new cases of TA-GVHD during this reporting period.

Cumulative data

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

Figure 16

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



COMMENTARY

- There has been a sharp drop in the number of cases of TA-GVHD reported annually since the period 1998-99. Leucodepletion of all blood components was introduced by the UK Blood Services in 1999. It is likely that this has reduced the risk of GVHD but the single case report in 2000-2001 demonstrates that a risk remains. This condition has a very high mortality; death was reported in all 13 cases reported to SHOT in previous years.
- At present, gamma irradiation of blood components is the only accepted method to prevent TA-GVHD in susceptible individuals.¹⁷
- Eighty-one patients who had a requirement to receive irradiated blood but who did not receive it are identified in the Chapter relating to IBCT (chapter 4). Fortunately, none developed the condition.

RECOMMENDATIONS

- Gamma irradiation of blood components for those at risk of GVHD remains essential. BCSH Blood Transfusion Task Force Guidelines define groups requiring this prophylaxis.²¹
- Awareness of the potential for this condition 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. Provision of the BCSH/NBS patient card and leaflet, available from local blood centres in England, is also recommended.
- New chemo or immuno-therapeutic regimens must be evaluated for their potential to predispose individuals to TA-GVHD. Regular update of guidelines is required to include up to date recommendations relating to drugs and protocols with potent immunosuppressive effects.

Action: Clinicians prescribing purine analogues and administering blood transfusion; HTTs; pharmacists, pharmaceutical industry; suppliers of laboratory IT systems

11 Transfusion-Transmitted Infections

Definition of a Transfusion Transmitted Infection (TTI)

A report of an infection suspected to be due to transfusion was classified as a **transfusion-transmitted infection** if the following criteria were met at the end of the 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 have been contaminated with the agent of infection

Summary

Since 1995, blood centres in England, Wales and Northern Ireland have reported possible transfusion transmitted infections, of which they have been informed, to the NBS/Health Protection Agency Communicable Disease Surveillance Centre (HPA CDSC) Transfusion Transmitted Infection Surveillance scheme. A similar scheme has existed in Scotland since 1998; data from this are passed to the NBS/HPA scheme.

In 2003, 38 reports of possible transfusion transmitted infections in the UK were made to the surveillance scheme. After the investigation had been completed, 8 reports were classified as probable transfusion transmitted infections (2 HBV, 1 HIV, 1 HAV, 1 malaria and 3 bacterial contaminations) one of whom died, 24 were found not to be related to transfusion and 3 had an undetermined source. Full investigations on 2 cases are still pending. The UK's National CJD Surveillance Unit and the NBS made a report of the first possible case of transfusion transmitted vCJD, identified in 2003 following a death in a transfusion recipient. Additionally, there were 38 reports of post transfusion reactions (PTRs) in England, Wales and Northern Ireland where the packs were returned for investigation to exclude bacterial contamination, although this was not thought the likely cause of the reaction. No evidence of contamination was found in these 38 cases.

The risk of acquiring an infection through blood transfusion in the UK remains very low. The low number of reports of bacterial contaminations this year could be the result of improved donor arm cleaning and procedures to divert the first 20-30ml of each donation. However, transfusion transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of components. Continued reporting and investigation of all possible incidents of transfusion transmitted infections is essential.

Introduction

In the investigation of incidents of infection suspected to be due to transfusion, markers of infection in the implicated donation, or in subsequent samples from the donor(s) of the implicated donation(s), can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. The blood service must therefore be informed about implicated transfusions so that investigations can be conducted to confirm or refute the suspicion that the implicated transfusion(s) may have been infectious. This is essential to prevent further transmissions by other components of the same donation or future donations from chronically infected donors, or to reveal any systematic errors in laboratory testing, or transfusion practices.

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. 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. In addition, the occurrence of disease, or the observation of serological markers of infection in donors can lead to the ascertainment of TTIs through "lookback" - the tracing and testing of recipients exposed to components collected from donors during potentially infectious periods. Recipients may be asymptomatic at this time and only identified by this investigation.

A surveillance system to collect standardised information about infections suspected to have been transmitted by transfusion was introduced in the UK (excluding Scotland) and the Republic of Ireland as a collaboration between the transfusion services and the HPA CDSC in October 1995. A similar collation of reports of incidents investigated by Scottish blood centres has been in place in Scotland since October 1998. Data from the UK are included in this report.

Methods

Blood centres in England, Wales and Northern Ireland were asked to report possible incidents of infection due to transfusion of which they had been informed to the NBS/HPA CDSC Transfusion Transmitted Infection Surveillance, according to criteria listed in the Table 17. For each eligible incident, information about the recipient, the recipient's infection, the transfusion(s) implicated, and details of the findings of the investigation were collected using a detailed proforma. (See www.shot-uk.org for a specimen proforma).

Classification of reports

After investigations were closed, reported incidents were classified as a TTI according to the definition given at the beginning of this chapter. Incidents in which the infection in the recipient was shown not to be due to transfusion, since all donations were cleared or another source of infection was identified, were classified as not transfusion transmitted infections. Incidents were classified as undetermined if the investigation was closed without being able to conclusively confirm or refute that blood transfusion was the source of the infection. If, during the investigation, another possible source of infection was identified or the recipient was found to have a pre-existing infection, the incident was excluded.

Table 17

The inclusion and exclusion criteria for reporting eligible incidents of infection suspected to be due to transfusion to the NBS/HPA CDSC Transfusion Transmitted Infection Surveillance

Inclusion criteria:

An incident should be reported if receipt of the transfusion is confirmed, and either,

- a) The infection in the recipient had been confirmed by detection of antibody, antigen, RNA/DNA or culture as appropriate and there was no evidence that the recipient was infected prior to transfusion

Or,

- b) The recipient had acute clinical hepatitis of no known cause (including no evidence of acute hepatitis A virus (HAV), HBV, HCV, Epstein-Barr virus or CMV infection in post-transfusion samples to date).

Exclusion criteria:

An incident should NOT be reported if:

- a) The incident involved HCV or HIV in recipients who had received transfusions in the UK prior to routine testing. [September 1991 for anti-HCV, October 1985 for anti-HIV] [±]
- b) The incident involved HTLV in a recipient identified through the HTLV National Lookback ^{±±}
- c) The incident involved a transfusion outside UK

[±] The blood service is rarely able to conduct follow-up investigation of all untested donors implicated in post-transfusion HCV or HIV incidents, and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions. ^{±±}Any post-transfusion HTLV infections identified through the HTLV National Lookback are excluded but will be collated, analysed and published elsewhere, as was done previously with HCV 'lookback'.

Data received by 31/3/2004 about incidents of suspected transfusion-transmitted infections initially reported by blood centres between 1/1/2003 and 31/12/2003 are included in this report. Data received about incidents reported during the previous seven years of the surveillance system are included in the cumulative table and figure.

Blood centres in Scotland reported all incidents to the Microbiology Reference Unit of the Scottish Blood Transfusion Service where they were investigated, and the details and conclusion of each case was then provided to the SHOT system.

Results

Between 1/1/2003 and 31/12/2003, 38 reports were made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance: 29 from blood centres in England, Wales and Northern Ireland and 8 from Scotland (Figure 17). All 12 of the blood centres in England, Wales and Northern Ireland, and all 5 centres in Scotland made reports. An additional report of a possible transfusion transmitted vCJD was made by the UK's National CJD Surveillance Unit and the National Blood Service.

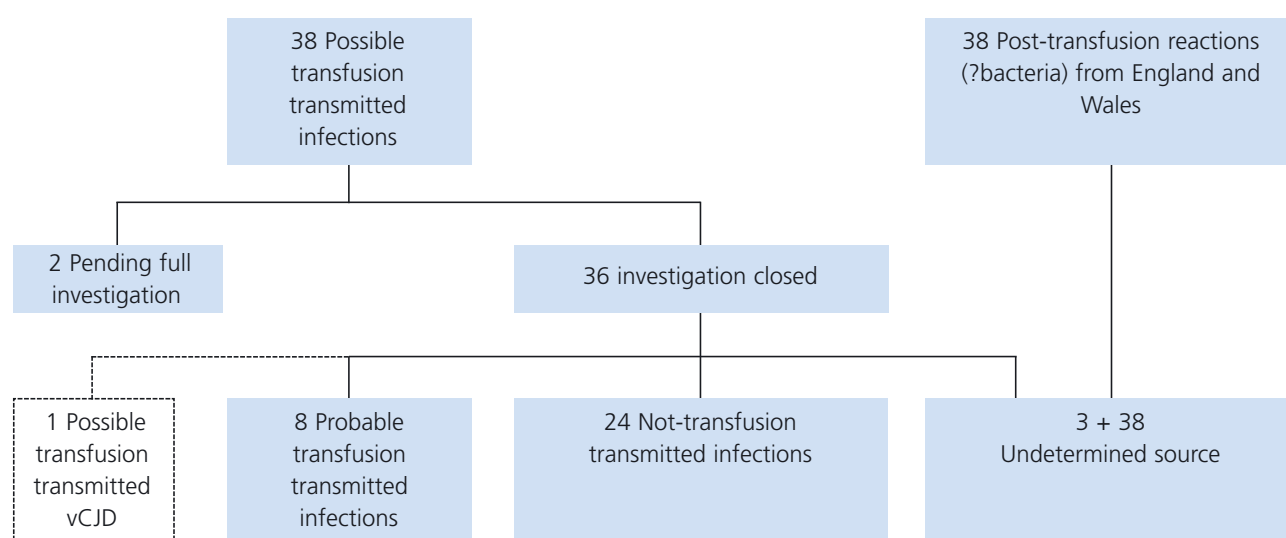
Of the 29 reports from blood centres in England, Wales and Northern Ireland, six (22%) were classified as transfusion-transmitted infections: one due to HAV, one due to HBV, one due to HIV, one due to malaria and two due to bacterial contaminations. For 20 (74%) reports (11 bacteraemia, 4 HBV infections, 3 HCV infections, 1 HIV infection, 1 CMV), investigation was complete and there was no evidence to implicate transfusion as the source of infection, these were classified as not transfusion transmitted infections. Two reports of incidents were classified as HCV infections of undetermined source due to inconclusive investigation of the donation(s) implicated as the source of infection. A further HCV infection suspected to be due to transfusion was still pending full investigation.

An additional 38 reports were made from blood centres in England, Wales and Northern Ireland of PTRs where bacterial contamination was initially included in the differential diagnosis, but had no evidence of bacterial infection in either the recipient or the implicated component that could have caused the reaction.

In Scotland, blood centres made eight reports of infection suspected to be due to transfusion during 2003. Two reports (1 HBV and 1 *Escherichia coli*) were classified as transfusion transmitted infection following complete investigations. For two HBV, two HCV and one parvovirus infection investigations were complete and there was no evidence to implicate transfusion as the source of infection. One HCV infection suspected to be due to transfusion is still under investigation. Scottish cases reported since October 1998 have been included in the numbers of post-transfusion infections and transfusion-transmitted infections shown in the tables and figures here since the 2000/01 SHOT Annual report.

Figure 17

Classification of reports made to the NBS/HPA CDSC Transfusion Transmitted Infection Surveillance from blood centres in the UK between 1/1/2003 and 31/12/2003.



Details of transfusion-transmitted infections

A. Infections for which donation testing was mandatory

Hepatitis B virus

Two transfusion transmitted HBV infections were reported during 2003.

A previously Hepatitis B surface antigen (HBsAg) negative apheresis donor was found to be positive after routine testing in February 2003. An archived sample of a donation made a month earlier was re-tested and found to be HBsAg, anti-Hepatitis B core (HBc) and HBV DNA negative. A single recipient (two year old female) of this donation was traced, tested and monitored. Six months following the transfusion of the implicated unit she was found to be HBsAg and HBV DNA positive. Sequencing information linked the infection in the donor to the recipient, thus the source of the recipient's infection was confirmed to be probably due to an HBV infectious donation from a donor in the very early acute phase of infection.

A recipient (57 year old male) developed symptoms of acute hepatitis five months after receiving 2 units of red cells during surgery in 2002. The recipient was found to be HBsAg and anti-HBc IgM positive and the archived samples of both units were tested; one was found to be HBsAg, anti-HBc (total) and HBV DNA positive, the other was negative for all markers of HBV infection. The recipient's infection was concluded to be probably due to an HBV infectious unit of red cells from a first time donor in the acute phase of infection with HBsAg at a low level that had not been detected by the HBsAg assay. The donor of the implicated unit was unaware of his infection and had donated again six months later (before investigation had commenced). By this time, the donor's infection had resolved and so the unit tested negative at the routine HBsAg test and was transfused. A single recipient of the second donation was traced and tested, but there was no evidence of transmission; the archive sample of this donation was found to be HBsAg and HBV DNA negative and anti-HBc (total) positive.

Hepatitis C virus

No transfusion transmitted HCV infections were reported during this year.

HIV

One transfusion transmitted HIV infection was detected by lookback in 2003. A previously anti-HIV negative donor was found to be positive by routine testing of a donation in 2003. The archive of the previous anti-HIV negative donation made in 2002 was retrieved for PCR testing and found to be HIV RNA positive. A single recipient (female, 45 years) was traced and tested 15 months after transfusion of the red cells from the donation following post-operative bleeding and found to be anti-HIV and HIV RNA positive. The recipient reported having had an illness consistent with HIV seroconversion three weeks after transfusion, however had no other symptoms when identified as HIV positive. The probable source of the recipient's infection was concluded to be an HIV infectious unit of red cells from a seroconverting donor. No source of the donor's infection was identified.

A further incident of predicted HIV transmission from a seroconverting donor was identified in 2003. Here, an anti-HIV negative donation (donated in October 2002) was found to be HIV RNA positive by retrospective PCR testing performed because the donor was anti-HIV positive at the time of the subsequent donation. Red cells from the seronegative unit had been transfused to a recipient (a female aged over 80 years), who had received a single unit of red cells during surgery for a fractured femur in 2002. The recipient died soon after surgery, and her HIV status was not determined.

In both of the above cases, the level of viraemia in the implicated donation was sufficient to have been detected by pooled PCR testing, although this is not currently part of routine testing in England and Wales.

HTLV

No transfusion transmitted HTLV infections were reported during this year.

B. Infections for which donation testing was not mandatory

Hepatitis A

One transfusion-transmitted HAV infection report was made in 2003. A repeat donor reported onset of jaundice 6 days after making a donation in 2000. The donor was tested, found to be anti-HAV IgM positive and made a complete recovery. The donation had been processed: platelets were included in a pool; the plasma from the infected donor was not used and the red cells discarded. The recipient of the platelet pool (32 year old female) had received a bone marrow transplant 6 weeks prior to the transfusion and was known to be anti-HAV IgG and IgM negative at that time.

Four weeks following transfusion, the recipient was found to be anti-HAV IgG positive but HAV IgM negative. The anti-HAV IgG reactivity was initially thought to be due to the high dose of Human Normal Immunoglobulin (HNIG) the recipient was given following realisation she had been exposed to HAV. A further 4 weeks later the recipient was tested and found to be anti-HAV IgM positive, and subsequently developed symptoms of hepatitis A disease, but later recovered. The probable source of the recipient's infection was concluded to be an HAV infectious unit of pooled platelets.

Malaria

One transfusion-transmitted malaria infection report was made in 2003. Low haemoglobin levels in a recipient (51 year old male) following transfusion over a period of three months for treatment of sickle cell disease prompted an investigation into the probable cause. Review of a blood film from the recipient identified a low-level *Plasmodium falciparum* parasitaemia despite a lack of travel outside the UK. The archived samples of the seven units of red cells received by the recipient were retrieved and tested for malaria antibodies and the donors were contacted for any relevant travel history. One of the seven units had been tested prior to transfusion because the donor reported relevant travel history at the time of donation, and was negative, and was also found negative on re-testing. Five of the remaining six units were negative for malaria antibodies; all except one of these donors had no relevant travel history. The seventh donation tested positive for malaria antibodies: the donor had lived in West Africa until the age of 21, although had not visited the area for seven years prior to the donation. The probable source of the recipient's infection was concluded to be a *P.falciparum* infected unit of red cells. Although malaria antibody testing would have avoided this transmission, the donor did not qualify for testing under current guidelines.

Bacterial contamination

Three transfusion-transmitted bacterial contaminations were reported between 1/1/2003 and 31/12/2003. Two recipients had major morbidity, and one died.

One recipient (42 year old male) developed rigors and hypotension following transfusion of a two-day old unit of apheresis platelets for treatment of leukaemia in Scotland in 2003. The patient was resuscitated with intra-venous fluids and given antibiotics but went on to develop a fever and symptoms of cardiac failure. The patient was transferred to intensive care for monitoring, but died 15 hours after the transfusion. *E.coli* was cultured from the recipient's blood and the implicated platelet pack. Extensive investigation failed to reveal a source for the bacterial contamination, but since the venepuncture site of the donor was not swabbed, the donor's arm could not be excluded as a possible source. The probable source of the recipient's infection was concluded to be a unit of apheresis platelets contaminated with *E.coli* of unknown source.

One recipient (60 year old female) developed fever and diarrhoea following transfusion of a single unit of 4-day-old apheresis platelets during treatment for acute myeloid leukaemia. *Staphylococcus aureus* of the identical strain was cultured from the recipient's blood, the platelet pack and the venepuncture site of the donor. The recipient recovered after antibiotic treatment and was discharged from hospital five days after the transfusion. The probable source of the recipient's infection was concluded to be a unit of platelets contaminated with *S. aureus* from the donor's arm.

One recipient (61 year old male) developed hypotension, breathlessness, fever and rigors following a transfusion of a 5-day old unit of pooled platelets. *Staphylococcus epidermidis* was cultured from the patient, the pooled unit and (although not same strain) the venepuncture site of one of the donors. The probable source of the recipient's infection was concluded to be a unit of pooled platelets contaminated with *S. epidermidis*. The most likely source of the contamination was the donor's arm despite the fact that the organism isolated was a different strain from that isolated from the patient and the platelet pack.

vCJD

The first possible case of transfusion transmitted vCJD was identified during 2003 by the UK's National CJD Surveillance Unit and the NBS.⁷ The details of the case were passed to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance and have been included here. In 2003, a case of vCJD was diagnosed after death in a transfusion recipient (aged 62 years).⁷ In 1996, this individual had received a unit of red cells from a donor who developed symptoms of vCJD 3 years later and died from pathologically confirmed vCJD in 2000. The implicated red cell unit was not leucodepleted and had been given to the recipient during a transfusion of 5 units of red cells while undergoing surgery. The source of the recipient's infection was concluded to possibly be a vCJD infectious unit of red cells. Due to the absence of further evidence that human prions can be transmitted by transfusion, and because (in this case) other possible sources such as dietary exposure to Bovine Spongiform Encephalopathy agent could not be excluded, the source of the recipient's infection could not be confirmed as transfusion.

Under-reporting

Each year, incidents of post-transfusion infection may be missed. However, the extent of under-reporting is unknown. Incidents ascertained by this surveillance system were diagnosed infections or reactions, suspected to be attributable to transfusion, communicated to the blood service and from there passed to the surveillance unit; failure at any one of these steps may result in under-reporting. The proportion of post-transfusion infections that are reported may vary between year as other factors such as testing performed on transfusion recipients, awareness of transfusion as a possible source of infection, reporting of information to blood centres and reporting of information from blood centres to the surveillance centre vary.

Previous year – 2001/2002

In the previous year's SHOT Annual Report, of 34 reports made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance Post-transfusion Infection Surveillance between 01/10/2002 to 31/12/2002, five (15%) of these were subsequently classified as TTIs (see SHOT Annual Report 2001-02 for details). Two reports of investigations that were classified as pending full investigation in the 2001-02 SHOT Annual Report have been concluded not to be as a result of transfusion as all donations were cleared, and subsequently classified as not transfusion transmitted infections.

Cumulative data

The cumulative number of reports of PTI and PTR made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance by year of transfusion since October 1995 is shown in Figure 18. The cumulative numbers of reports of TTIs made by year of transfusion reported by the end of December 2003 are shown in Table 18.

Figure 18

Reports of possible transfusion transmitted infection in UK and post-transfusion reaction in England and Wales made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance by year of report (Scotland included from 10/98)

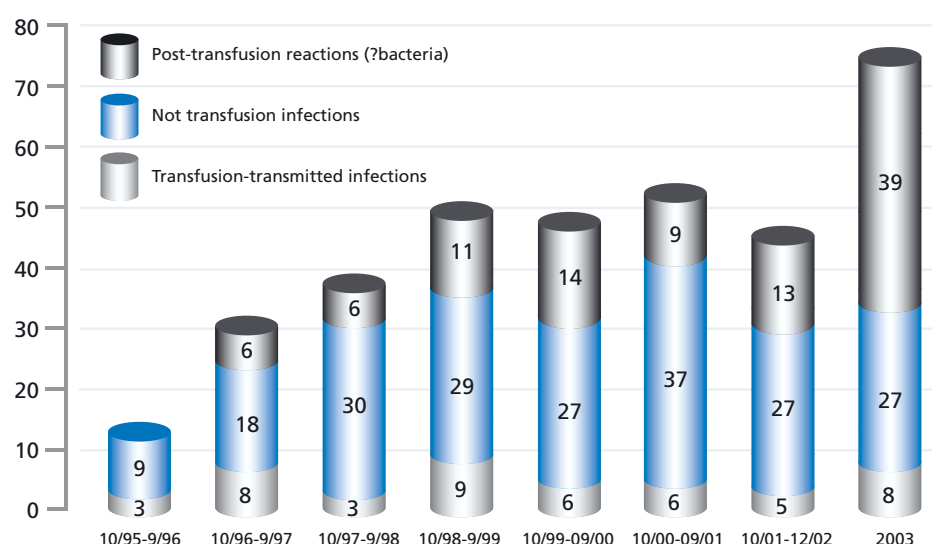


Table 18

Cumulative total of reports of transfusion-transmitted infections made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance between 1/10/1995-31/12/2003 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	Pre 1996	1996	1997	1998	1999	2000	2001	2002	2003	Total	Deaths
Infection											
HAV	-	1(1)	-	-	-	1 (1)	-	-		2	-
HBV	2(2) ^b	1(1)	1(1)	1(1)	2(3)	1(1)	-	1(1)	1(1)	10	-
HCV	-	1(1)	1(1)	-	-	-	-	-		2	-
HIVc	-	1(3)	-	-	-	-	-	1(1)		2	-
Bacteria	1(1)	1(1)	3(3)	4(4) ^{ax2}	4(4) ^a	7(7) ^{ax3}	5(5)	1(1)	3(3) ^a	29	7
Malaria	-	-	1(1) ^a	-	-	-	-	-	1(1)	2	1
HTLV I	2(2)	-	-	-	-	-	-	-		2	-
Possible vCJD		1(1)								1	1
Total	5(5)^b	6(8)	6(6)^a	5(5)^{ax2}	6(6)^a	9(9)	5(5)	3(3)	5(5)	50	9

Notes: ^a Infection was implicated in the death of a recipient.

^b One household member who was caring for the recipient has been diagnosed with acute HBV.

^c One additional investigation failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.

Cumulative data about bacterial transmissions

A summary of the species of bacteria and the type and age of the implicated components for the 29 transfusion-transmitted bacterial contaminations reported between 01/10/1995 and 31/12/2003 are shown in table 19.

Table 19

Reports of transfusion-transmitted bacterial contaminations in UK made to NBS/HPA CDSC Transfusion Transmitted Infection Surveillance between 01/10/1995 and 31/12/2003 by species and component type and age (N=29).

	Platelets Age (in days) at use							Red cells
	1	2	3	4	5	NK	ALL	
All species	0	2	3	6	10	4	25	4
<i>Bacillus cereus</i>				3 ^a		1	4	
<i>Coagulase negative Staphylococci</i>					1		1	1 (23 days)
<i>Enterobacter aerogenes</i>			1 ^a				1	
<i>Escherichia coli</i>		1 ^a	1 ^a			1	3	
<i>group B Streptococcus</i>			1	1		1	3	
<i>Morganella morganii</i>					1		1	
<i>Serratia liquifaciens</i>								1
<i>Staphylococcus aureus</i>					2	1 ^a	3	
<i>Staphylococcus epidermidis</i>		1 ^a		2	6		9	1 (32 days)
<i>Yersinia entercolitica</i>								1 ^a (33 days)

^a Infection was implicated in the death of a recipient.

Nine of the 25 contaminated platelet units were collected by apheresis from single donors, 15 were recovered from whole blood donations (each from pooling of four donations) and for one the source of platelets was not specified. For 10 of these cases, the donor's arm was confirmed by subsequent testing to have been the probable source of the contamination. For some others, investigation of donors' arms was incomplete or inconclusive but the nature of the contaminating organism was suggestive of a skin contaminant that was most likely to have been introduced to the pack at the time of collection. For 2 cases, the donor's blood was concluded to have been the source of the contamination (i.e. endogenous bacteria, so contamination of the pack not preventable by skin cleansing or diversion).

Cumulative data about Hepatitis B virus transmissions

Nine of the ten reports of transfusion-transmitted HBV infections in the UK made since October 1995 have been concluded to be probably due to infectious blood collected from donors with acute HBV infection, with only one (reported in the first reporting year) due to infectious blood from a donor with later stage HBV infection. This is a change from that observed in earlier collations of transfusion-transmitted HBV. For example, between 1991 and 1997 only three of 14 transfusion-transmitted HBV infections reported to the Health Protection Agency were found to be due to donations from donors with acute infection, with the majority being due to donations from donors with chronic infection²². This change has implications for possible options to further reduce the risk of transfusion-transmitted HBV infection. The value of anti-HBc screening for detection of subliminal HBsAg at the end of carriage has declined, and the very sensitive HBsAg assays now in use lessen the potential additional yield which would be gained from HBV DNA testing.

COMMENTARY

- A total of 76 reports of incidents involving infections suspected to be due to transfusion were made to the NBS/HPA CDSC Transfusion Transmitted Infection Surveillance in 2003, the highest number of reports since the scheme began in 1995. Eight (11%) of the reports were concluded to be probably due to transfusion of an infectious unit of blood; three due to bacteria, four due to viruses and one due to malaria. One report was of the first possible case of transfusion transmitted vCJD.
- Each year, the number of transfusion-transmitted infections reported is small and fluctuations are to be expected. Also, the reporting system is probably biased towards ascertainment of investigations of infections that cause rapid onset of acute disease such as bacteria; in the cumulative data bacteria have accounted for the majority (62%) of reported transmissions by transfusion and the majority (88%) of known deaths due to transfusion transmitted infections.
- For two of the three reports of transfusion transmitted bacterial infection, the probable source was confirmed to be the donor's arm. This suggests that arm cleansing was inadequate to deal with the bacterial load. [despite improved cleansing protocol]. It is of interest that the low number of cases of transfusion transmitted bacterial infection in 2003 has followed the implementation of the strategy to divert the first 20-30 mL of the donation in 2002. The low number is unlikely to be due to under-ascertainment as a high number of reports of investigations of suspected bacterial infection have been received suggesting enhanced awareness and reporting of possible bacterial transmissions. This observation requires confirmation from continuing surveillance in future years. Improved arm cleansing and methods for testing platelets for bacterial contamination are being considered to further reduce the risk of bacterial contamination.
- Many of the 38 reports of PTR incidents (in England, Wales and Northern Ireland) involved cases where bacterial contamination was not clinically felt the most likely diagnosis, but the packs were returned for culture for the sake of completeness. In 2 cases, bacteria were isolated from the recipient but there was no evidence to implicate transfusion as the source of infection. In occasional cases full investigation was not possible because appropriate samples were not available. Conclusive investigation of a suspected bacteraemia in a transfusion recipient relies heavily on the collection and handling of relevant samples at the hospital where the transfusion was performed. It is recommended that hospitals seek advice from their local blood centre to ensure that cases are properly investigated.
- During 2003, reports were made of both transfusion transmitted HIV and HBV infections. The risk of an HIV or HBV infectious donation entering the blood supply still remains very low in the presence of the current routine testing protocol of blood donations; these include highly sensitive combined anti-HIV plus antigen assays and also HBsAg assays. The absence of any reports of transfusion transmitted HCV infections is consistent with the expected low risk of an HCV infectious donation entering the blood supply in the presence of anti-HCV and HCV RNA testing.

- The ascertainment of infection in 3 donors (HIV, HBV, HAV) led to the tracing and testing of recipients exposed to components collected during their potentially infectious periods. Recipients were initially asymptomatic at this time and may only have been identified by these investigations. This illustrates the importance of post-donation information and the need to act on it.
- In 2003, the first possible incident of transfusion-transmitted vCJD was reported. Human prion disease may be transmissible via blood transfusion, but this report represents only a single case of vCJD in a transfusion recipient and further evidence is required before the source can be confirmed. Precautions are currently in place to reduce the risk of transmission through blood transfusion. These include leucodepletion of all blood components (since 1999), the use of virally inactivated FFP obtained outside the UK for vulnerable groups (children born after 1st January 1996), importation of plasma for fractionation (since 1998) and the exclusion of donors who have received a blood transfusion in the UK since 1980 (implemented in April 2004).
- 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 and HBV infections to assess the need for additional testing methods, such as HIV RNA testing or anti-HBc. SAC Care and Selection of Donors ensures donor deferral criteria is optimal in terms of exclusion of donors with behaviour that may put them at high risk of infections.

RECOMMENDATIONS

- Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components. These include:
 - Continuation of diversion of the first 20-30 mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site)
 - Careful attention to adequate cleansing of donors' arms
 - Adherence to BCSH guidelines (1999)¹⁴ with regard to the visual inspection of blood components for any irregular appearance immediately prior to transfusion.
- UK Blood Services should continue to review and implement options available to minimise the risk of bacterial contamination of platelets.
- Hospitals should consult guidelines and the blood service about the investigation of transfusion reactions suspected to be due to bacteria. Attention should be paid to the sampling and storage of implicated units.
- Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately.

12 Serious Hazards of Transfusion Events Reported in Patients Less Than 18 Years of Age

DEFINITION

This section describes all validated cases of serious transfusion complications reported to SHOT involving a patient less than 18 years of age.

A total of 449 analysable reports were received by SHOT for the 12-month period January to December 2003. Of these 59 involved patients less than 18 years of age (13%). During the period October 1996 to the end of December 2002 (6 years and 3 months) 141 validated cases were reported (8.65% of all analysable reports). The increase this year in the number of reported adverse events is more likely to reflect a greater awareness by the paediatric community of blood transfusion safety issues and the requirement to report errors to SHOT due to the establishment of multi-speciality Hospital Transfusion and Clinical Risk Management Committees than a true increase in reportable events. This chapter deals with the findings from 59 completed questionnaires. A further 4 reported cases were withdrawn; 1 because of an incomplete questionnaire, 1 because the criteria was not met and 2 because the transfusion was required for an obstetric cause and did not take place on a paediatric ward.

Last year the SHOT report acknowledged that in paediatric practice the transfusion of blood and blood components is concentrated to a small number of high user specialities, primarily neonatal medicine, ECMO, haemato-oncology, intensive care and cardiac surgery. These patient groups often have specific requirements for component selection and specification. Outwith high demand specialities the transfusion of blood is uncommon in children and this may lead to a lack of expertise. Both of these situations may be associated with an increased potential for error, which would be reflected in the IBCT category. Last year the analyses of reported cases for patients less than 18 years of age showed the distribution category of adverse events to be roughly similar to that seen over all age groups with the exception of DHTR and PTP, both of which were less common in children. For the year 2003, IBCT episodes were proportionally commoner in children, particularly infants, whilst DHTR, TA-GVHD, PTP and TTI events were not reported. One case in a 3 year-old initially reported as a DHTR was re-classified as IBCT following further investigation. Twenty-eight of 348 (8%) of IBCT incidents occurred in patients less than 12 months of age. The percentage of red cells transfused to this group has been reported in an epidemiology study to be 1.2%⁸ suggesting a relatively higher incidence of IBCT errors in this age group (see chapter 4 IBCT).

AGE

Age was highly relevant. 29/59 (49%) of cases occurred in infants less than 1 year of age, of whom 20/29 (69%) were in their 1st month of life. This reflects the pattern of transfusion in the paediatric population, in particular the relative high incidence of transfusion in the neonate because of the complications of prematurity and congenital malformation. All but one reported events in infants less than 1 year of life were within the IBCT category, which in turn reflects the requirement for special consideration of blood component selection in the infant and neonate. The relative incidences of the two commonest reported events, IBCT and ATR, were similar across the paediatric age group after the first year of life. Confirmed TRALI events were not reported in the first year of life and PTP and TA-GVHD were not reported at all in patients less than 18 years of age (Table 20). There was 1 reported case of HBV transmission to a 2 year old but since the reporting system for TTI is different, the case is not reported here. See TTI chapter 11 for details.

Table 20

	No of Cases	Incident Type					
Age		IBCT	ATR	DTR	TRALI	TA-GVHD	TTI
Birth - 1month	20	20					
1 month - 1 year	9	8	1				
1 -5 years	13	12			1		
5 -10 years	3	2	1				
>10 year	14	11	1		2		
Total	59	53	3		3		

OUTCOME

There were no deaths due to transfusion related events amongst the 59 reported cases, but there were 4 deaths from unrelated causes.

Nine patients suffered significant morbidity or are at risk of future problems due to RhD sensitisation. These included 5 cases of haemolysis from ABO incompatible products and 2 RhD negative females who received RhD positive blood and who therefore may be sensitised and have problems in future pregnancies (see IBCT Chapter 4). One 18 month old child was significantly over transfused and one neonate was exchange transfused with blood prepared for an intrauterine transfusion (IUT).

Table 21 Cases of transfusion related morbidity

Case no.	Component	Group of component	Group of patient	Error	Outcome
1) 10mths	SD FFP	Group O	Not tested	Laboratory Group O SD FFP issued.	Haemolysis requiring transfusion
2) 4mth	Platelets and Cryo	Group O	Group A	Laboratory Large volumes of Group O platelets and Cryo issued and transfused	Probable haemolysis
3) 17yrs	RBC	Patient Group	Not Stated	Laboratory RBC of patient rather than recipient group issued for ABO mismatched BMT patient	Mild haemolysis
4) 1d	RBC	Group A	Group A	Laboratory Group A RBC issued for Group A infant of Group O mother Mild ABO HDN diagnosed retrospectively	Severe haemolytic transfusion reaction. Required exchange transfusion with Group O RBCs
5) 3yrs	RBC and Platelets	Group A1 RBC; Group O platelets	Group A2	Laboratory/Ward "Emergency" Group O platelets administered Group A1 RBCs transfused Anti-A1 in donor platelets caused haemolysis	Haemolysis
6) 2yrs	RBC	B RhD pos	B RhD neg	Laboratory	Possible sensitisation
7) 12yrs	RBC	A RhD pos	A RhD neg	Laboratory	Possible RhD sensitisation. Required exchange transfusion and anti-D IgG
8) 1d	RBC	-	-	Ward/collection Infant previously had an IUT. Blood for IUT taken from satellite and used for exchange transfusion.	Major morbidity. Respiratory failure, hepatic failure and poor perfusion.
9) 18mths	RBC	-	-	Request/administration Blood prescribed in units rather than mls.	Over-transfusion requiring venesection and saline infusion

INCORRECT BLOOD COMPONENT TRANSFUSED (N=53)

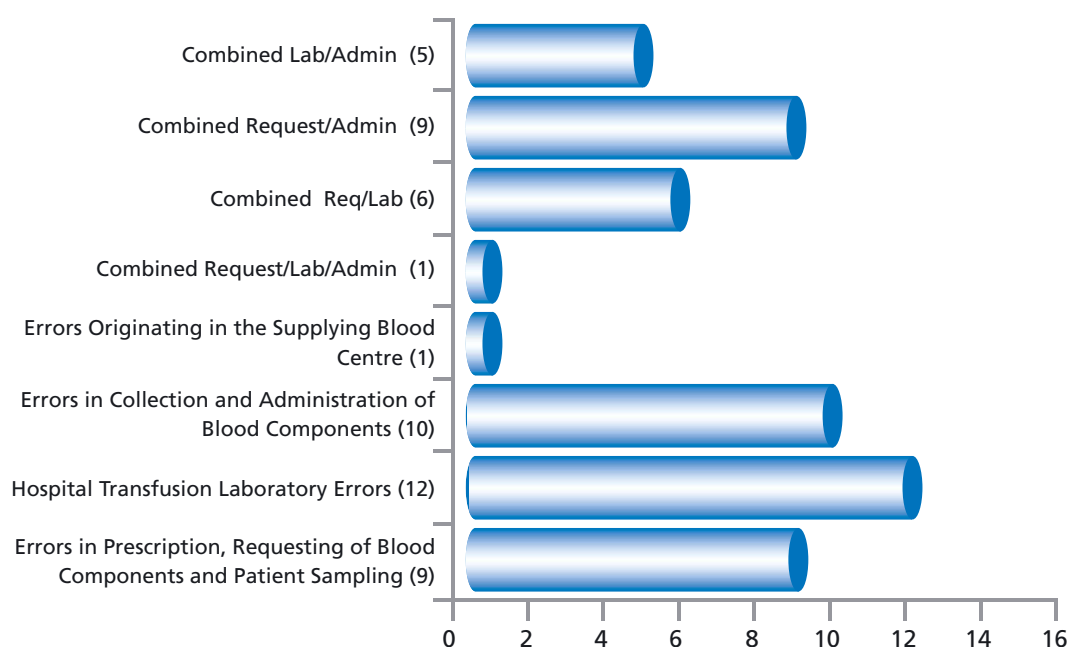
There were 53 errors in this category in patients less than 18 years of age. Two additional teenage females have been excluded because they were treated for obstetric problems and would not have been managed on a paediatric ward and 1 case was excluded because of an incomplete questionnaire.

DISTRIBUTION OF ERRORS

Figure 19 shows the distribution, according to the main reporting categories, of the 53 validated reports. Twenty-three of the 53 reported errors of IBCT involved multiple errors (44%) and in a significant number more than two departments contributed to the error or failed to perform an appropriate check.

Figure 19

Distribution of errors



OUTCOME IN IBCT GROUP

- Forty patients suffered no sequelae as a result of receiving an incorrect blood product.
- Nine patients suffered morbidity or potential morbidity but recovered and this group included 5 patients who developed intra-vascular haemolysis and 2 RhD negative females who received RhD positive red cells.
- Four patients died of their underlying condition.

DETAILS OF IBCT ERRORS

- The commonest error, 25 of 53 cases, involved the **failure to request/issue blood/blood component of appropriate specification**. These included
 - failure to request/issue irradiated blood/blood component (10 cases),
 - failure to request/issue CMV negative blood/blood product (3 cases),
 - failure to request/issue irradiated/CMV negative blood/blood products (4 cases),
 - issue/administration of non-MB FFP to children born after 1996 (7 cases)
 - wrong platelet product (1 case).

Four of the seven cases of failure to provide MB FFP involved children greater than one year of age suggesting that laboratory/clinical staff were not familiar with the DOH guideline on FFP administration to children born after 1996. There is also clearly a lack of awareness of the indications for CMV negative and irradiated blood and blood products in children.

- There were 9 cases that involved a patient receiving the **wrong blood/blood product due to misidentification in sampling, requesting, collection or administration**. Two of these involved telephone requests. Satellite refrigerators were also implicated in collection errors.

Case 10

Baby A and baby B were born on the same day. Baby A required transfusion, baby B did not. The SHO labelled the sample and request form with baby B details and verbally requested blood for baby B. The laboratory used baby B mother's sample for pre-transfusion testing and selected Group O Rh D negative blood which was transfused to baby A.

Whilst this infant came to no harm, the misidentification of patients can lead to fatal ABO incompatible transfusions. Children and infants in particular are at risk from errors arising from the misidentification at the time of sampling and administration because they cannot identify themselves verbally. The wearing and checking of wristbands are essential in the paediatric age group and may be the last opportunity to identify an error arising earlier in the transfusion chain.¹⁴

Case 11

Baby A in SCBU required a platelet transfusion. The SHO requested by telephone platelets for baby B and these were supplied and transfused to baby B.

Case 12

A 2 month old infant whose mother had Von Willebrand's disease (vWD) was to receive platelets. The request from the SHO was made by telephone. The laboratory recorded a request for and issued FFP which was transfused to the patient.

These two cases illustrate the need for care in identifying both the correct patient and the correct component. The risk of error may be greater when a written request is not involved and requests are made by telephone.

Case 13

A 1-day old infant had had a previous IUT. Blood crossmatched for an IUT was taken from a satellite refrigerator and used for exchange transfusion. The infant suffered major morbidity including respiratory failure, poor perfusion and hepatic failure.

This case illustrates the need for staff involved with these patients to be aware of the specific requirements for blood for exchange transfusion and IUT, both of which are uncommon procedures.

- There were 3 reports in which the wrong component was transfused, but these involved the use of "adult" blood from satellite refrigerators in emergency situations for neonates.
- Two patients received the **wrong group of product post-ABO mismatched bone marrow transplant** for different reasons. The wrong group of FFP was requested for one patient in a shared care setting because of failure of appropriate communication. These patients are at high risk of such errors and should carry patient held records or adequate communication should be guaranteed. The second error occurred in a 17-year old who was given RBC of his own blood group rather than those of the donor. This highlights the need for an alert and check system in the laboratory for all patients with complex transfusion requirements and education of laboratory and medical staff.
- Three children were **over-transfused** due to a miscalculation of their transfusion requirements.

Case 14

An 18-month old with a teratoma was to have a routine transfusion overnight. The SHO requested and prescribed "3 units" of blood believing that the laboratory would provide paediatric packs. The laboratory issued standard units. The infant was transfused overnight but the next morning the day staff stopped the transfusion when they noted the child to be plethoric. The child's haemoglobin was 216g/L and required venesection and a saline infusion.

This report raises a number of issues, the most important of which is that blood for children should be prescribed by volume and not in units. Paediatric packs are not recommended for this child's age group. Secondly, routine transfusion should not take place during the night when nursing staff levels are low. Thirdly, experienced staff might have realised that this volume of transfusion was inappropriate for a child of this age.

- On 5 occasions blood/blood components were transfused which had **expired or had been stored inappropriately**.

Case 15

An 8-day old post-operative cardiac baby received an expired unit of blood. The expired unit had been returned to the laboratory for discard but remained labelled. A doctor removed the expired blood from the laboratory and transfused it to the infant.

Expired blood should never be transfused and in this particular case could have led to hyperkalaemia with significant sequelae. The checking procedure pre-transfusion should include the expiry date of the unit and this error should have been detected at the bedside check.

- The number of **serological laboratory errors** was small (4 cases). A Group AB patient was grouped as a Group A and therefore had no consequence. The second error involved a failure to detect a maternal anti-c, which was of significance because her 2-day old pre-term infant was transfused Group O red blood.

Case 16

A 2-year old Group B RhD negative girl received group O RhD positive RBC because of a Rh D grouping error in the laboratory. This has the potential for rhesus sensitisation and very serious consequences for pregnancies in the future.

Case 17

A 21-day old pre-term infant became DAT positive with spherocytes on his blood film after receiving blood labelled "high titre negative for neonate" which was later found to have high titre IgG anti- A,B.

This serves to remind us that Transfusion Service testing for high titre anti A/B cannot confidently exclude all high titre donations.

- There were 3 reports of **Group O platelets or cryoprecipitate given to Group A patients** both of whom had subsequent haemolysis. At least one patient received large volumes of platelets. Group A individuals should receive group specific platelets but because of supply difficulties may receive group O platelets, provided that these components lack high titre anti-A.

Case 18

A 1 day old group A infant with undiagnosed mild ABO haemolytic disease of the newborn (HDN) - made retrospectively - was transfused group A red cells. The infant's mother was group O and the infant suffered severe haemolysis and required exchange transfusion with group O blood.

Whilst a serious event, mild ABO HDN can be difficult to diagnose.

Case 19

A 3-year old male with neuroblastoma whose parents applied pressure to the ward staff to give platelets overnight to facilitate early discharge. Emergency group O platelets were given at a dose of 25mL/kg instead of 15mL/kg. The child, who was group A2, was also transfused with Group A 1 red cells and developed haemolysis. This was thought to be due to anti-A1 in the group O platelet donor.

This case illustrates a number of points. Group O platelets were used instead of group specific platelets because of their ready availability and parental/patient pressure took precedent over best practice. The increased dose of platelets may have contributed to the haemolysis by providing a greater amount of anti-A1.

OUTCOME OF IBCT

Twenty-one episodes of IBCT involved emergency requests/transfusion, 30 were during routine hours and for 2 there was inadequate information.

IMMUNOLOGICAL COMPLICATIONS

Acute Transfusion Reactions (N=3)

Age range: 4 months – 12 years.

Components transfused: Platelet concentrates in all 3 cases

Aetiology of reaction – 2 were allergic reactions for which no cause was identified.
1 haemolytic reaction.

Case 20

A 4-month old group A infant was supported on ECMO following repair of a VSD. She received large volumes of group O platelets when group A platelets could not be supplied by the Blood Transfusion service. There was clinical and laboratory evidence of haemolysis within 24 hours and anti- A was eluted from her red cells. Whilst this infant subsequently died this was not as a direct result of haemolysis.

No patient had sequelae directly related to the acute transfusion reaction.

Transfusion-Related Acute Lung Injury (N=3)

There were four cases of TRALI reported, one of which was not validated and three of which are reported in chapter 8.

COMMENTARY

- 29/59 (49%) of cases occurred in infants less than 1 year of age, with 20/29 of these (69%) involving infants in their first month of life. This reflects the pattern of transfusion in the paediatric population, in particular the relative high incidence of transfusion in the neonate because of the complications of prematurity and congenital malformations.
- Patients across the paediatric age spectrum often require special consideration of component selection or manipulation because of age and/or underlying diagnosis/intervention. 25 of the 53 cases of IBCT related to a failure to request or issue the blood or blood components of the correct specification. There were 7 cases of failure to issue MB FFP to children within the required age group. It is clear from some of the reported errors that there is lack of awareness amongst laboratory, nursing and medical staff of the special needs of paediatric recipients of blood and blood components.
- Care must be taken in the selection of ABO compatible plasma products as there were 3 cases where group O platelets or FFP caused haemolysis in group A individuals.
- Errors arise due to failure to identify patients at the time of sampling and administration. Wristband checks are of paramount importance in younger children who are unable to identify themselves verbally.
- Delayed transfusion reactions are rare in children and TA-GVHD, PTP and TTI were not reported.

RECOMMENDATIONS

- Laboratory, nursing and medical staff should all be aware of the special consideration of component selection and/or requirement for product manipulation for neonatal and paediatric transfusion. Specific education of these staff in paediatric transfusion practice is crucial.

Action: HTTs

- The wearing and checking of wrist or ankle name bands is essential in the paediatric age group, who may not be able to identify themselves verbally, and may be the last opportunity to identify an error arising earlier in the transfusion chain.

Action: Staff of paediatric units

- The recent BCSH transfusion guideline for neonates and older children⁹ states that group A recipients should receive group A platelets, but accepts that group O can be transfused as a second alternative provided that these components are lacking high titre anti-A. However, Transfusion Service testing for high titre anti-A cannot confidently exclude all high titre anti A donors and they should be encouraged to ensure that Group A platelets are always available for these patients.

Action: UK Transfusion Services

- The importance of good and accurate communication at every level in transfusion practice must be emphasised to prevent unnecessary error.

Action: All involved in the transfusion process

13 Adverse Events Relating to Autologous Transfusion

SHOT has received no reports this year of adverse reactions relating to autologous pre-deposit donation. Although the use of this technique has fallen in recent years, previous studies have estimated that the incidence of associated adverse events is approximately 2.6%²³ suggesting that there is under-reporting to SHOT.

There have been three reports of adverse events relating to the re-infusion of autologous blood. Two of these are included in the IBCT chapter and one as an ATR (case 8). The two IBCT cases are summarised below.

Case 1

A 40 year old woman was admitted for a renal transplant. Prior to operation she had donated 3 units of autologous blood, which was stored in the hospital blood bank. There was no documentation either in the patient's notes or the laboratory to alert staff that autologous blood was available. When the laboratory received a request for 2 units of red cells, they provided allogeneic blood, one unit of which was transfused during the operation. Only when the expired autologous blood was discovered in the blood bank stock refrigerator was the error recognised. The hospital has since instituted a system whereby alerts are placed in the patient's laboratory record and hospital notes when autologous blood is available.

This patient was exposed to risk in two ways; firstly her haemoglobin level was reduced by the removal of three units of blood, so that she was more likely to require peri-operative transfusion, and she was then unnecessarily exposed to allogeneic blood because of poor communication.

Case 2

An unrelated volunteer bone marrow donor was receiving his predonated autologous blood post-operatively when nursing staff noted that the in-line filter had become blocked. Closer inspection of the unit revealed the presence of multiple small clots. These had not been noticed by the laboratory or by the nurses who checked the unit before administration. The transfusion was abandoned. There was no harm to the patient.

The reporter did not state whether the pre-deposited unit had been collected by the blood service or by the hospital. This case highlights the importance of correct handling of autologous pre-deposited blood. The EU Directive on blood safety, which is due to become law in February, requires that autologous blood is subject to the same regulations as homologous blood.

Case 3

See ATR chapter 6, case 8

Strategies for blood conservation include the use of blood salvage in appropriate circumstances. With increasing use of these technologies it is important that adverse events are reported and documented, so that the relative risks of alternatives to allogeneic blood transfusion can be assessed. SHOT is therefore keen to receive reports of problems associated with all modalities of autologous transfusion. Defects of blood salvage devices should also be reported to the MHRA.

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