SERIOUS HAZARDS OF TRANSFUSION

SHOT

Annual Report 2005

Affiliated to the Royal College of Pathologists

British Blood Transfusion Society, British Society for Haematology
Faculty of Public Health Medicine, Institute of Biomedical Science
NHS Confederation, Health Protection Agency Centre for Infections
Royal College of Anaesthetists, Royal College of Nursing
Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Physicians, Royal College of Surgeons,
The four UK Blood Services

SERIOUS HAZARDS OF TRANSFUSION

ANNUAL REPORT

2005

Affiliated to the Royal College of Pathologists

British Blood Transfusion Society, British Society for Haematology

Faculty of Public Health Medicine, Institute of Biomedical Science

NHS Confederation, Health Protection Agency Centre for Infections

Royal College of Anaesthetists, Royal College of Nursing

Royal College of Obstetricians and Gynaecologists

Royal College of Paediatrics and Child Health

Royal College of Physicians, Royal College of Surgeons, The four UK Blood Services

Published 30th November 2006

by The Serious Hazards of Transfusion Steering Group

National Co-ordinators:	Dr Dorothy Stainsby
	Ms Katy Davison (HPA Centre for Infections)
Scheme Manager:	Mrs Hilary Jones (SHOT office)
Data Collection Specialist:	Mrs Aysha Boncinelli (SHOT Office)

Standing Working Group

Stainsby D*	Jones H*	Cohen H*	Asher D*
Atterbury C*	Boncinelli A*	Brant L *	Chaffe W
Chapman C E*	Davison K	Gerrard R	Gray A
Knowles S*	Milkins C*	Norfolk D R*	Taylor C

** Writing Group members*

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
Enquiries: shot@nbs.nhs.uk

ISBN 0 9532 789 8 0

Infectious hazards

Ms. Katy Davison

Clinical Scientist

HPA Centre for Infections

61 Colindale Avenue

London NW9 5EQ

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

Contents

		Page
1.	KEYNOTE MESSAGE	**6**
2.	SUMMARY OF FINDINGS AND RECOMMENDATIONS	**8**
3.	PROGRESS REPORT ON PREVIOUS RECOMMENDATIONS	**13**
4.	OVERVIEW OF RESULTS 2005	**16**
5.	INCORRECT BLOOD COMPONENT TRANSFUSED	**20**
6.	NEAR MISS EVENTS	**40**
7.	ACUTE TRANSFUSION REACTIONS	**45**
8.	DELAYED TRANSFUSION REACTIONS	**54**
9.	TRANSFUSION-RELATED ACUTE LUNG INJURY	**63**
10.	POST-TRANSFUSION PURPURA	**73**
11.	TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE	**75**
12.	TRANSFUSION TRANSMITTED INFECTIONS	**77**
13.	ACKNOWLEDGEMENTS	**81**
14.	REFERENCES	**82**

Glossary of Terms

ACE	Angiotensin-converting enzyme
AHG	Antihuman globulin
AHTR	Acute haemolytic transfusion reaction
ALG	Antilymphocyte globulin
ALI	Acute lung injury
APTT	Activated partial thromboplastin time
ARDS	Acute respiratory distress syndrome
ATR	Acute transfusion reaction
BBTS ASM	British Blood Transfusion Society Annual Scientific Meeting
BCSH	British Committee for Standards in Haematology
BMS	Biomedical scientist
BSE	Bovine spongiform encephalopathy
BSMS	Blood Stocks Management Scheme
CCU	Coronary care unit
CEO	Chief Executive Officer
CfH	Connecting for Health
CMO	Chief Medical Officer
CMV	Cytomegalovirus
CXR	Chest x-ray
DAT	Direct antiglobulin test
DH	Department of Health
DHTR	Delayed haemolytic transfusion reaction
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid
DTR	Delayed transfusion reaction
EDTA	Ethylenediaminetetraacetic acid
ELISA	Enzyme-linked immunosorbent assay
EU	European Union
FBC	Full blood count
FFP	Fresh frozen plasma
GI	Gastrointestinal
GP	General practitioner
HAV	Hepatitis A virus
HBc	Hepatitis B core
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HDN	Haemolytic disease of the newborn
HDU	High dependency unit
HELPP	Haemolysis, elevated liver enzyme levels and a low platelet count
HHV-8	Human herpes virus
HIV	Human immunodeficiency virus
HLA	Human leucocyte antigen
HPA	Human platelet antigens
HPA	Health Protection Agency

Glossary of Terms

HSC	Health Service circular
HTC	Hospital transfusion committee
HTLV	Human T-cell leukaemia virus
HTT	Hospital transfusion team
IAT	Indirect antiglobulin test
IBCT	Incorrect blood component transfused
ICU	Intensive care unit
Ig	Immunoglobulin
IV	Intravenous
JPAC	Joint Professional Advisory Committee
LISS	Low-ionic-strength-solution
MHRA	Medicines and Healthcare products Regulatory Agency
MLA	Medical laboratory assistant
NAITP	Neonatal alloimmune thrombocytopenic purpura
NBS	National Blood Service
NBTC	National Blood Transfusion Committee (England)
NHL	Non Hodgkins Lymphoma
NHS	National Health Service
NIBSC	National Institute for Biological Standards and Control
NPSA	National Patient Safety Agency
ODA	Operating department assistant
PAD	Preoperative autologous donation
PBSC	Peripheral blood stem cell
PCR	Polymerase chain reaction
PFGE	Pulsed-field gel electrophoresis
PNH	Paroxysmal nocturnal haemoglobinuria
PSM	Platelet suspension medium
PTP	Post-transfusion purpura
RAADP	Routine antenatal anti-D prophylaxis
RAST	Radioallergosorbent test
RBRP	Right blood to right patient
RCI	Red cell immunology
RDW	Red cell distribution width
RNA	Ribonucleic acid
SABRE	Serious adverse blood reactions and events
SAC	Standing advisory committee
SACTTI	Standing advisory committee, transfusion transmitted infection
SpR	Specialist Registrar
TACO	Transfusion associated circulatory overload
TA-GvHD	Transfusion associated – Graft versus host disease
TRALI	Transfusion related acute lung injury
TTI	Transfusion transmitted infection
TTP	Thrombotic thrombocytopenic purpura
UKBTS	UK blood transfusion services
vCJD	Variant Creutzfeldt Jakob disease

1 Keynote Messages

Improvements in patient safety

There are some encouraging messages to be found in this year's SHOT report. The number of ABO incompatible transfusions has fallen from 19 in 2004 to 10 in 2005, an all-time low and a 54% reduction since 2001/2002. The reasons for this are complex, but the vitally important contribution of transfusion practitioners, as recommended by SHOT [1] and HSC 2002/009 'Better Blood Transfusion' [2] to patient safety must be acknowledged and appreciated. The recent National Comparative Audit of Transfusion[3] indicated that 75% of the 270 responding hospitals in the UK have a transfusion practitioner in post, thus there remains scope for further improvement.

The collaborative project between SHOT, the Chief Medical Officer's National Blood Transfusion Committee (NBTC) and the National Patient Safety Agency (NPSA), aimed at reducing blood administration errors, promises to consolidate this improvement by ensuring the competency of all staff involved in blood transfusion. The NPSA/SHOT/NBTC Safer Practice Notice 'Right patient, right blood' [4] also requires Trusts to risk assess their transfusion process and ensure that the final patient identification check is carried out next to the patient, by matching the blood pack with the patient's wristband or personal identifier. These must be worn by every patient.[5] A further important outcome of this project has been the bringing together of the IT Working Groups of the NPSA and NBTC, the Connecting for Health (CfH) 'Do Once and Share' (DOAS) Blood Transfusion project, SHOT and the British Committee for Standards in Haematology (BCSH) Transfusion Taskforce in a collaborative project to develop a standard specification for electronic tracking of the transfusion process, based on the process map developed by DOAS. This initiative represents the start of a structured national approach to the use of IT in blood transfusion as recommended in previous SHOT reports.

This year's report also documents the reduction in cases of immune-mediated Transfusion Related Acute Lung Injury (TRALI) following implementation by the UK Blood Services of a policy of using male donors, as far as possible, for fresh frozen plasma (FFP) and the plasma contribution to platelet pools. Since its inception, SHOT has called for a national over-arching body with responsibility for prioritising blood safety initiatives. This is still awaited, but in its absence the blood services have taken note of SHOT findings and worked towards reducing preventable risks, notably TRALI and bacterial contamination of platelets.

SHOT welcomes the ongoing commitment of the Chief Medical Officers to transfusion safety and looks forward to the forthcoming 'Better Blood Transfusion 3' initiative.

Reporting to SHOT

This year, reports of events, reactions and near misses were received from 69% of hospitals. Comparison with data on red cell issues from the Blood Stocks Management Scheme[6] (BSMS) over a 3-year period 2003-2005 enables benchmarking of SHOT reporting, which will be fed back to individual hospitals over the next few months. Opportunities exist for further exploration of data sharing, in collaboration with hospitals.

Open reporting without fear has been a cornerstone of SHOT since its inception and must continue to be preserved and encouraged. This philosophy, strongly promoted by the NPSA as an 'open and fair culture', does not absolve individuals from professional responsibility and accountability, but emphasises the need for healthcare professionals and organisations to explore the underlying reasons for errors within a supportive environment, with the ultimate aim of improving patient care and safety.[7] This approach must be extended into the new organisations that are evolving in the NHS. A punitive blame culture is destructive and counterproductive.

Laboratory initiative

The focus of SHOT in recent years has been on improving the safety of blood administration at the bedside. However, errors in hospital transfusion laboratories occurred in 37% of incorrect blood component transfused (IBCT) cases reported in 2005. The SHOT plenary session at the British Blood Transfusion Society (BBTS) Annual Scientific Meeting (ASM) in December 2005 highlighted some of the underlying reasons for laboratory errors and identified the need for a national initiative to support improvements in practice. Additionally the Blood Safety and Quality Regulations[8] require hospital transfusion laboratories to implement quality systems and demonstrate continuous quality improvement. SHOT is collaborating in an initiative, led by the Institute of Biomedical Science (IBMS) and involving other relevant professional bodies, aimed at improving standards in laboratories, and hence reducing errors. The current move by the IBMS to develop Consultant Biomedical Scientist (BMS) posts is an important step forward in the move to enhance transfusion practice.

As a first step, a stakeholder workshop is planned for 7th March 2007.

Near miss

SHOT recognises the importance of information from near miss events. Internal reporting and investigation of near misses is a requirement of HSC 2002/009 'Better Blood Transfusion',[2] but, although the number of these events received by SHOT has increased year-on-year, only 55% of hospitals reported them this year. Following a survey of near miss events and a workshop on 21st November 2006 we will be 're-launching' near miss reporting in 2007, with the intention of improving the quality of information gained from these events.

Priorities for the future

The UK Blood Safety and Quality Regulations[8], implemented on 8th November 2005, have had a major impact on hospital transfusion laboratories and also on SHOT. Hospitals are now reporting electronically, using the Serious Adverse Blood Reactions and Events (SABRE) system developed by the Medicines and Healthcare Products Regulatory Agency (MHRA), and the monitoring of reports received suggests that the transition has been successful. Compliance with the new regulations presents challenges for hospital laboratories, but also opportunities to drive improvements.

Discussions are ongoing between SHOT, MHRA, the UK Blood Services, National Blood Transfusion Committees and the Department of Health, to clarify the respective roles and responsibilities of SHOT and MHRA. It is essential that a structure is established that enables UK haemovigilance to flourish and the UK's international recognition in this field to be preserved.

Dr Hannah Cohen MD FRCP FRCPath

Chair, SHOT Steering Group

Dr Dorothy Stainsby FRCP FRCPath

SHOT National Medical Co-ordinator

2 Summary of Findings and Recommendations

Participation

Two hundred and seventy-nine of 403 eligible hospitals in the UK submitted at least one appropriate report, or near miss, giving an overall participation rate of 69%.

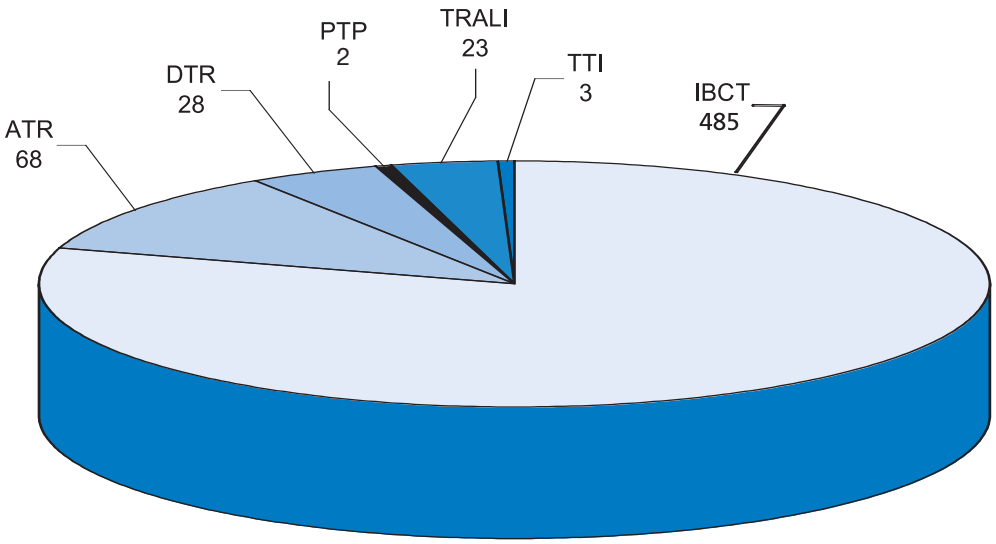
Of the 124 non-reporting hospitals, 1 is a high red cell user by the BSMS criteria (i.e. >11,000 units p.a.) and 7 are moderate users (6,000 to 11,000 units) although 2 of these are bordering on the high category. Sixty-seven hospitals are low users (<6,000 units p.a.). No data were available for the remaining 49 non-reporting hospitals most of which receive their stocks via other hospitals. Feedback on participation will be provided to individual hospitals.

Total events reported

The 2005 report includes data from 609 cases, including 3 transfusion transmitted infection (TTI) reports received from the NBS/Health Protection Agency Centre for Infections Surveillance (NBS/HPA CIS). A further report of probable variant Creutzfeldt Jakob disease (vCJD) transmission has also been included.

Figure 1

Breakdown of reports received in 2005 (n=609)



Transfusion related mortality

There were 5 transfusion related deaths. In 1 case involving an ABO incompatible red cell transfusion (case 1, chapter 5 of the full report) there was certain and conclusive evidence that death was related to transfusion (imputability 3). In another, caused by an anaphylactic reaction to FFP (case 10, chapter 7), the evidence was clearly in favour (imputability 2). In 2 patients, death was possibly due to TRALI (cases 7 and 13 in the TRALI tables available on the SHOT website www.shot-uk.org) and 1 patient (case 17, chapter 5) died possibly related to overtransfusion (all 3 cases, imputability 1).

Incorrect blood component transfused ("wrong blood") incidents

Four hundred and eighty-five reports were analysed, of which 481 (99%) were 'no-harm' events in which the patient suffered minor or no morbidity. These reports were analysed in 7 sub-groups, summarised in Table 1.

Table 1

Types of events

Type of event	Number (%)
'Wrong blood' events where a patient received a blood component intended for a different patient or of an incorrect group.	87 (18%)
Other pre-transfusion testing errors – including incorrect D groups, missed allo-antibodies and missed serological incompatibility.	22 (4.5%)
Blood of the incorrect group given to recipients of ABO mismatched PBSC or bone marrow transplant.	2 (0.5%)
Failure to provide blood of appropriate specification or that did not meet the patient's special requirements.	141 (29%)
Inappropriate or unnecessary transfusions.	67 (14%)
'Unsafe' transfusion where there were handling or storage errors.	79 (16%)
Events relating to administration of anti-D immunoglobulin.	87 (18%)
Total	**485**

In each sub-group, the contribution of errors in clinical areas and in laboratories was assessed.

In 50/87 (57%) 'wrong blood' cases, in which 115 separate errors were identified, the pre-transfusion checking procedure was carried out incorrectly or omitted altogether.

Hospital transfusion laboratory errors occurred in 179/485 (37%) of all cases.

There were 169 IBCT reports in which an incorrect blood component was transfused due to a bedside administration error and the time of transfusion was known. Thirty-seven percent of these took place between 2000 hours and 0800 hours. These data were compared with an observational study on the time and location of blood transfusion carried out in 28 hospitals in the Northern and Yorkshire regions in September 2005 (H Tinegate, C Thompson, unpublished data), which found that 28.5% of red cell units were transfused between 2000 hours and 0800 hours, indicating that blood transfusions outside of core hours are inherently less safe.

Near miss events

SHOT defines 'near miss' as 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. 1358 near miss incidents were reported during 2005, an increase of 26% compared to 2004. A further 204 reports were reported as error logs from 3 hospitals.

As in previous years, patient mis-identification at the blood sampling stage resulting in 'wrong blood in tube' was the most frequently reported event, accounting for 574/1358 (42.2%) of reports.

Transfusion related acute lung injury (TRALI)

Twenty-three case reports of suspected TRALI were analysed in 2005, of which 6 were considered highly likely or probable (imputability 2-3) and the diagnosis was supported by the finding of a relevant antibody in the donor. In none of these 6 cases was FFP the implicated component. Three were related to platelets (1 pool and 2 apheresis), 2 to red cells and 1 to cryoprecipitate. In all 6 cases the donor of the implicated component was female.

Other immune reactions

There were 68 analysable reports of acute transfusion reactions (ATR) of which 5 were haemolytic, 25 anaphylactic, 28 severe allergic, 7 hypotensive or unclassifiable and 3 febrile. Twenty-three reactions were due to red cells, 24 to FFP and 19 to platelets. It is of particular concern that, in 8/24 (33%) of the adverse reactions to FFP, including one fatality and 2 cases of serious morbidity, there did not appear to be a clear clinical indication for FFP use.

Twenty-eight delayed haemolytic transfusion reactions (DHTR) were analysed. Six patients were asymptomatic and 22 had evidence of increased red cell destruction but without renal impairment.

There were 2 reports of post-transfusion purpura (PTP) and no reported case of transfusion-associated graft-versus-host disease (TA-GvHD).

There were no reports of reactions associated with reinfusion of autologous blood.

Transfusion transmitted infections

Forty-six reports of suspected transfusion transmitted infections were made from blood centres throughout the UK (41 in England and Wales and 5 in Scotland) to the NBS/HPA Centre for Infection Surveillance during 2005. Three reports, 1 of hepatitis B (HBV) transmission and 2 cases of bacterial contamination of platelets, were confirmed as TTIs. In addition there were 2 reports of predicted hepatitis A (HAV) transmission. A further report was received from the Health Protection Agency of a clinical diagnosis of vCJD in a blood transfusion recipient.

SHOT RECOMMENDATIONS 2005

Formulation of these recommendations has included consultation with stakeholders, in response to feedback last year from the National Blood Transfusion Committee. This consultation process will be further developed in the future and it is hoped that it will strengthen support for the recommendations and ensure implementation.

Specific recommendations relevant to individual chapters and learning points from IBCT events can be found in the main report and on the website, and will also be included in educational material aimed at specific professional groups, which will be developed and distributed during the year.

Recommendations made in previous reports remain active, and progress against these is summarised in Chapter 3. In particular, SHOT continues to support a nationally co-ordinated initiative to evaluate information technology, and the establishment of an over-arching body to prioritise transfusion safety initiatives.

The ultimate responsibility for implementation of SHOT recommendations in hospitals lies with their respective Chief Executive Officers (CEOs). However, the day-to-day responsibility is likely to be delegated to the consultant haematologist with responsibility for transfusion, together with the Hospital Transfusion Committee (HTC) and Hospital Transfusion Team (HTT). The introduction of transfusion practitioners and multidisciplinary HTTs with adequate staffing and support underpins hospital transfusion safety. It is essential that transfusion safety is maintained as hospitals reprofile clinical services in response to financial and other organisational pressures.

1 **'Right patient – right blood':** This joint initiative between the NPSA, SHOT and the NBTC aims to reduce the risk of ABO incompatible transfusions by improving the safety of blood administration. Hospitals must act on the Safer Practice Notice 'Right patient right blood'[4] within the required timescale. A crucial element of this initiative, also required by the Blood Safety and Quality Regulations 2005,[8] is competency-based training, which must be implemented for all staff involved in the blood transfusion process. It is essential that hospital CEOs recognise that this is a necessary and ongoing process and will add to the workload of the HTT.

Action: Hospital CEOs.

2 **Appropriate use of blood components:** Considerable progress has been made in limiting unnecessary transfusion of red cells, but the use of FFP and platelets continues to rise. Acute transfusion reactions are more frequent following transfusion of plasma-rich components than red cells and this year in 8/24 (33%) of severe allergic or anaphylactic reactions to FFP, including one fatality and 2 cases of serious morbidity, there did not appear to be a clear clinical indication for FFP use.

Current national BCSH guidelines on the appropriate use of FFP and platelets[9,10] should be incorporated into local protocols that are readily available in relevant clinical and laboratory areas, included in induction and update training and subject to clinical audit.

Action: Consultant haematologists with responsibility for transfusion together with the HTC and HTT.

3 **Better laboratory practice:** Hospital laboratory errors occurred in 37% of all IBCT reports. An initiative aimed at improving practice in hospital transfusion laboratories is under way, led by the IBMS. In the meantime, local quality improvements must be supported and resources provided to underpin the development of quality systems. It is essential that the quality and responsiveness of hospital transfusion laboratories is maintained as Pathology Services in England face major reorganisation following the Carter Report,[11] with the possible development of independent Pathology Trusts and diversification of providers of pathology services.

Action: Hospital CEOs.

4 **Avoid blood transfusions outside of core hours:** Available data indicate that blood administration and pre-transfusion testing outside of core hours are less safe and should be avoided unless clinically essential. Hospitals planning to move to '24/7' working must employ adequate numbers of appropriately skilled clinical and laboratory staff to ensure transfusion safety. It may be useful to audit the occurrence of patient safety incidents in hospitals during different time periods.

Action: Hospital CEOs, consultant haematologists with responsibility for transfusion together with HTCs and HTTs.

5 **Investigation of serious transfusion reactions:** All serious transfusion reactions must be fully investigated. An update of BCSH guidelines is in progress.

Action: Consultant haematologists with responsibility for transfusion should implement current best practice.[12,13]

6 **Communication of complex transfusion requirements:** Failure to communicate special transfusion requirements is an important contributory factor in many cases of IBCT. Effective mechanisms must be developed for communication of information on complex transfusion requirements (e.g. for patients requiring irradiated components, those with allo-antibodies, stem-cell transplant recipients). The involvement of pharmacists in 'flagging' prescription of purine analogues is helpful in ensuring provision of irradiated components. Patient awareness and empowerment[14] should be encouraged. Organisations should work together to implement and where necessary develop appropriate tools (e.g. documentation for patients transferred between hospitals, patient held booklets, standard antibody cards with accompanying advice).

Action: UK National and Regional Blood Transfusion Committees to facilitate and coordinate, Hospital CEOs to implement.

7 **Increase safety of routine antenatal anti-D prophylaxis:** Reports of errors relating to anti-D immunoglobulin (Ig) administration are increasing, and 2 cases were reported in 2005 in which misinterpretation of the antenatal antibody investigation resulted in severe haemolytic disease of the fetus. Implementation of routine antenatal anti-D prophylaxis[15] must be supported by education of primary care clinicians and hospital laboratory staff. Current legislation[16] surrounding the issue and prescription of anti-D Ig requires clarification and is a potential source of system error. National guidelines[17] on antenatal testing must be incorporated into agreed local policies and subject to clinical audit.

Action: Royal Colleges of Midwives, General Practitioners, Obstetricians and Gynaecologists, Consultant haematologists, HTCs and HTTs.

8 **Further measures by the blood services to reduce TRALI and bacterial contamination:** Measures implemented thus far appear to have reduced the risks of TRALI and bacterial contamination of platelets. Further measures require evaluation including the implications for availability and efficacy of blood components as well as cost-effectiveness.

Action: UK Blood Services, Department of Health (DH) advisory mechanisms.

Recommendations for future developments

1 **Blood transfusion outside the hospital setting:** Against the background of a trend towards provision of care closer to the patient, there is a need for a standard of practice to be developed for transfusion in the community setting, including provision for appropriate management and reporting of adverse events.

Action: UK National Blood Transfusion Committees to facilitate and co-ordinate.

2 **Need for clinical studies:** There is a paucity of good quality randomised studies from which to develop evidence-based transfusion practice. Well designed clinical studies should be undertaken to answer some of the questions that arise in clinical practice, including the optimal methods of patient identification, systems organisation and appropriate blood product support in different clinical settings. This will require action from clinical researchers, statistical & analytical support and assistance from funding bodies.

Action: UK National Blood Transfusion Committees, UK Blood Services, Funding bodies e.g. Health Technology Assessment and National Institute for Healthcare Research.

3 **Future development of haemovigilance:** The implementation of the Blood Safety and Quality Regulations[8] provides a unique opportunity to develop and re-enforce haemovigilance in the UK. It is essential that a structure is established that enables UK haemovigilance to flourish and to maintain its international recognition.

Action: DH, UK Blood Services, UK National Blood Transfusion Committees.

3 Progress report on previous recommendations

Recommendations made in previous years remain pertinent, and the following table indicates what progress has been made. The earlier reports did not indicate responsibility for implementation, - for some recommendations this has been added retrospectively.

There is currently no effective mechanism for monitoring implementation of recommendations in hospitals.

Year first made	Recommendation	Target	Progress
2004	The RTC structure provides a potential forum for debate and sharing of problems and solutions in a supportive environment with expert clinical input. SHOT reportable incidents should be a standing agenda item for regional BMS forums and SPOT meetings. The RTCs should support translation of guidelines into local practice	RTCs and user groups	NBS Hospital Liaison teams focussed support on RTCs in 2005. RTCs setting up working groups in 2006
2004	Further national initiatives are needed to drive forward blood safety issues in hospital transfusion laboratories	NBTCs, with relevant professional bodies	Identified as a key recommendation in 2005. Launch of an initiative in 2007 led by IBMS aimed at improving laboratory practice
2003	Hospital transfusion laboratory staffing must be sufficient for safe transfusion practice	Trust CEOs	See above
2003	BCSH guidelines on transfusion of neonates and children should be implemented	RCPCH, RCN, staff in paediatric units and transfusion laboratories	SHOT 'Lessons for paediatric staff' in preparation. NBS Paediatric conference planned for Feb 2007
2003	The NBTCs and counterparts should take a pro-active lead in driving forward blood safety issues in hospitals	NBTCs	NBS Regional Hospital Transfusion Teams (Consultant, Nurse and Scientist) active in each region Parallel initiatives in Scotland, Wales and NI Educational tools developed
2002	HTTs must be established and supported	Trust CEOs	Survey in 2004 (M Murphy and C Howell) showed 70% of Trusts had HTT but only 30% were supported
2002	Blood transfusion must be in the curriculum for student nurses, medical undergraduates and newly qualified doctors	GMC, PMETB, Undergraduate Deans, NMC	An education subgroup of the NBTC has been established. This group is linking with Deans of Medical Schools and Universities to get transfusion included in their curricula. SNBTS training package www.learnbloodtransfusion.org.uk endorsed in Scotland, Wales and NI

Year first made	Recommendation	Target	Progress
2002	Blood transfusion should be in the curriculum of specialist trainees, especially anaesthetists and critical care nurses	Medical Royal Colleges, Universities	See above
2002	Blood transfusion should only be prescribed by authorised clinicians		Endorsed by CMO Annual Report 2003
2002	Mechanisms must be put in place for appropriate and timely communication of information regarding special requirements	NBTCs, Trust CEOs	Card now available for patients requiring irradiated components. Further work needed. Carried forward as key recommendation for 2005
2002	Resources must be made available in Trusts to ensure that appropriate and effective remedial action is taken following transfusion errors	SHAs, PCTs, Trust CEOs through HTCs and risk management structures	No mechanisms for monitoring
2002	SHOT recommendations must be on the clinical governance agenda	Trust CEOs	No mechanisms for monitoring
2001	An open learning and improvement culture must continue to be developed in which SHOT reporting is a key element	Trust CEOs	Philosophy supported by NPSA. SHOT has developed a training tool for root cause analysis
2001	An ongoing programme of education and training for all staff involved in transfusion	NBTCs and network, Trust CEOs, NPSA/NBTC/SHOT initiative	Mandated by NPSA SPN 'Right Patient, Right Blood'. Also a requirement of CNST standards. Educational tool www.learnbloodtransfusion.org.uk developed by SNBTS
2001	Appropriate use of blood components must be strenuously promoted and evaluated. This must include monitoring for serious adverse effects of alternatives to transfusion	NBTC, Trusts CEOs	Successive BBT initiatives promote this. NBS Appropriate Use Group and patients clinical team active. Red cell usage has fallen by >15% since 2000. The National Comparative Audit programme is auditing platelet use and use of blood in primary elective unilateral THR in 2006.
2001	Transfusion practitioners should be appointed in all trusts	Trust CEOs	Requirement of BBT2. Now appointed in 75% of hospitals (National Comparative Audit organisational audit 2005)
2001	More transfusion medical consultant time is needed in hospital trusts		Requirement of BBT2, but national shortage of consultant haematologists
2001	Existing procedures should be re-examined for flaws that could lead to systems errors		BCSH guidelines on Blood Administration currently under review.

Year first made	Recommendation	Target	Progress
2000	Basic epidemiological research is needed into the timing and location of transfusions in the hospital setting		Where and when study undertaken 2005 (H. Tinegate and C. Thompson)
1999	All institutions where blood is transfused must actively participate in SHOT	Trust CEOs	Requirement of BBT and CNST. Murphy and Howell survey indicated that 99% of responding hospitals (95% of NHS Trusts) participate. 69% reported events or near misses in 2005
1999	Education in blood transfusion must be included in the curriculum for all clinical staff involved in prescribing and administering blood. All staff involved in the transfusion chain in hospitals must receive appropriate training which must be documented. Effectiveness of training should be assessed by competency assessment.		See above
1998	IT as an aid to transfusion safety should be assessed and developed at national level.	NBTC IT WG, NPSA/NBTC/SHOT initiative, CfH	Co-ordination now achieved between NBTC, NPSA, CfH. National standard specification under development. Implementation is dependant on central funding through CfH or by individual Trusts
1997	There is a need for a national body with relevant expertise and resource to advise government on priorities for improvements in transfusion safety.	DH	MSBTO currently under review by DH. Outcome awaited

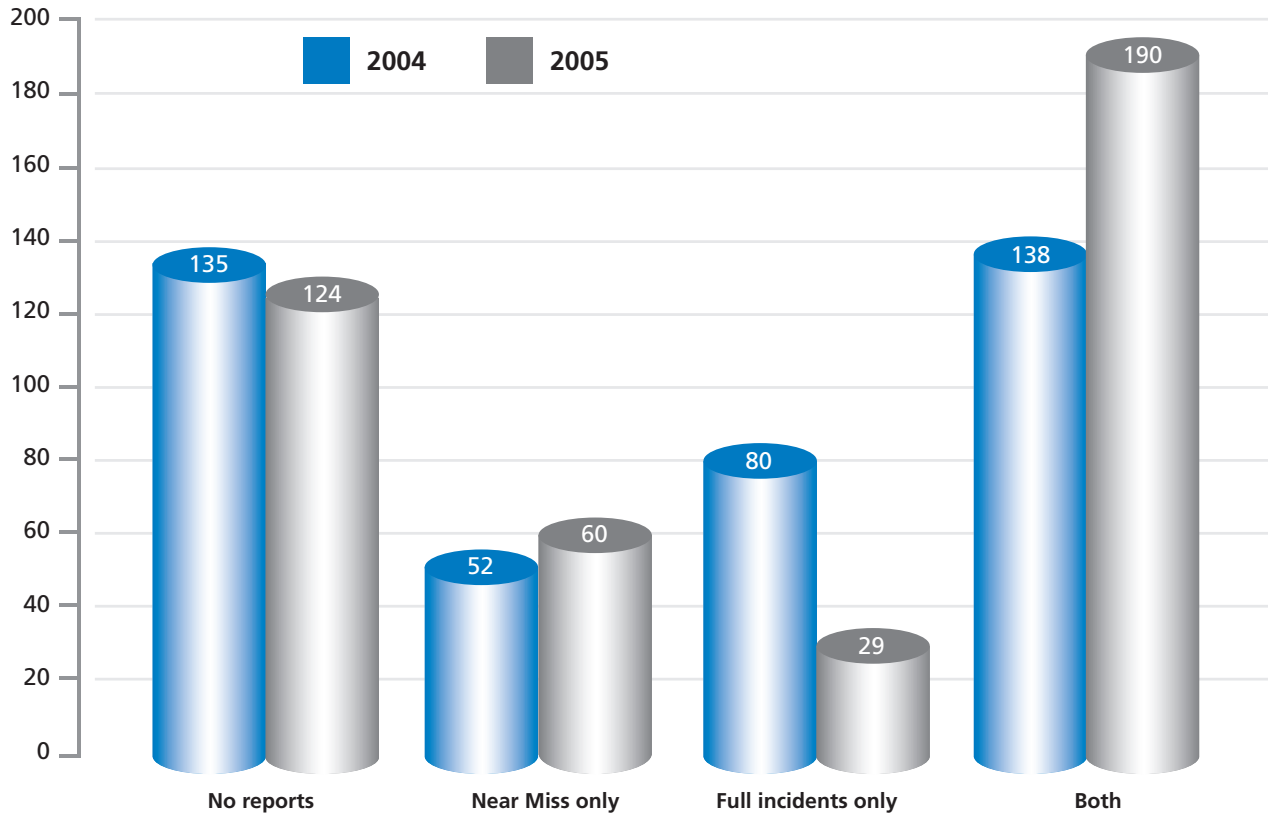
4 Overview of results 2005

This year's report analyses data collected between 1st January 2005 and 31st December 2005 inclusive.

Number of hospitals

The number of hospitals eligible to participate this year was 403. Two hundred and seventy-nine submitted at least one appropriate report, either a full incident or a near miss, making the overall participation rate 69% which is a slight increase on the 67% rate last year. If those hospitals which only reported near miss events are excluded, the participation rate falls to 54%. A breakdown of the types of incidents reported by hospitals is shown in Figure 2.

Figure 2
Breakdown of hospital reporting 2004 and 2005



Non-reporting hospitals

One hundred and twenty-four hospitals submitted no appropriate reports. Of these, 1 hospital is a high red cell consumer by the BSMS definition (i.e. >11,000 units p.a.) and 7 are moderate consumers (6,000 to 11,000 units) although 2 of the moderate consumers are bordering on the high category. Sixty-seven hospitals are low consumers (<6,000 units p.a.). No data were available for the remaining 49 non-reporting hospitals most of which receive their stocks via other hospitals.

The number of full incidents reported by each hospital varies considerably (minimum 1, maximum 16). This is shown graphically in figure 3.

Figure 3

Numbers of incidents reported by individual hospitals

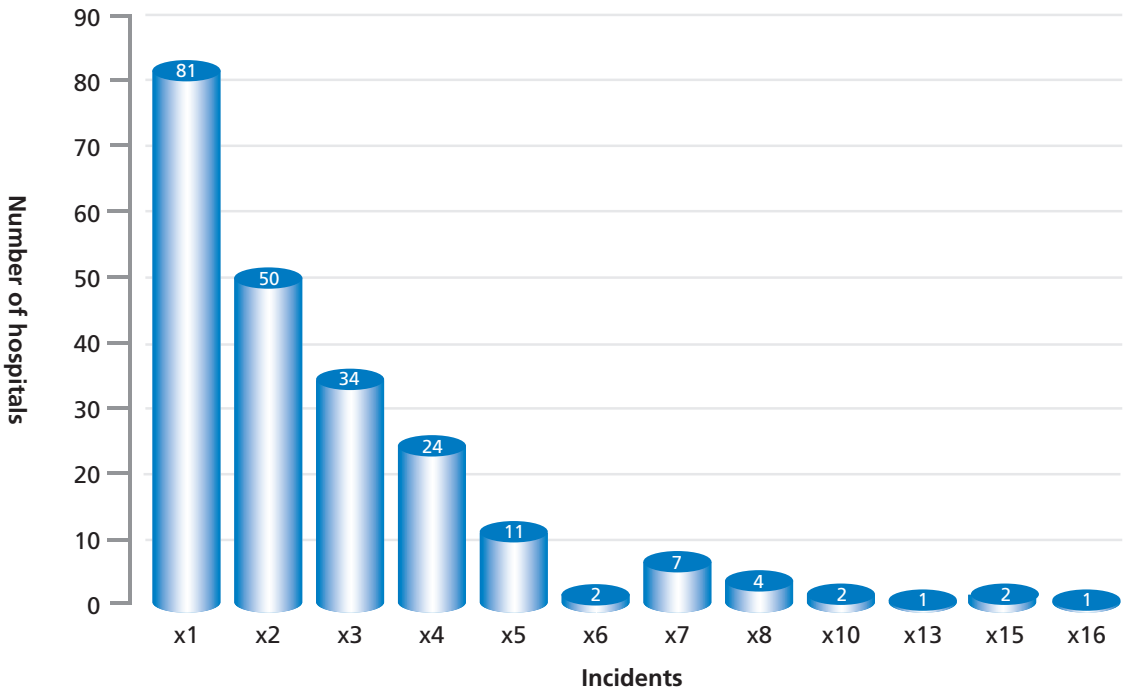


Table 2

Summary of completed questionnaires received.

	IBCT	ATR	DTR	PTP	TA-GvHD	TRALI	TTI	Totals
Questionnaires included in analysis	485	68	28	2	0	23	3	**609**

Numbers of components issued

Component issues are shown in table 3. There are currently no comprehensive data available on the numbers of transfusions carried out in the UK against which to measure the numbers of transfusion incidents. However figures from BSMS reveal that overall wastage of red cells in hospitals is only 2% making issue figures a useful proxy for blood usage.

Table 3

Total issues of blood components from the Transfusion Services of the UK in 2004/2005

Red Cells	**2,428,934**
Platelets	**258,528**
Fresh frozen plasma	**313,019**
Cryoprecipitate	**102,719**
TOTAL	**3,103,200**

Cumulative data 1996 - 2005

Figure 4

Numbers of incidents included in the analyses (n=3239)

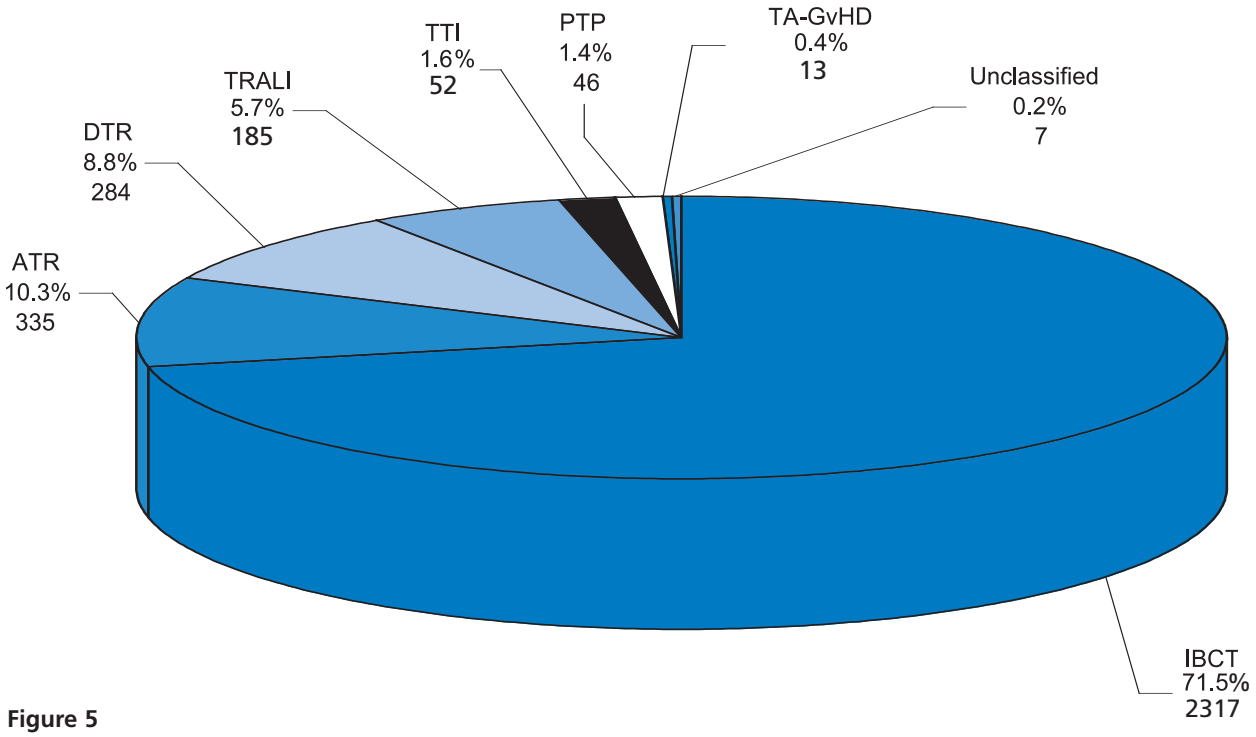


Figure 5

Comparison of report types reported 1996 - 2005

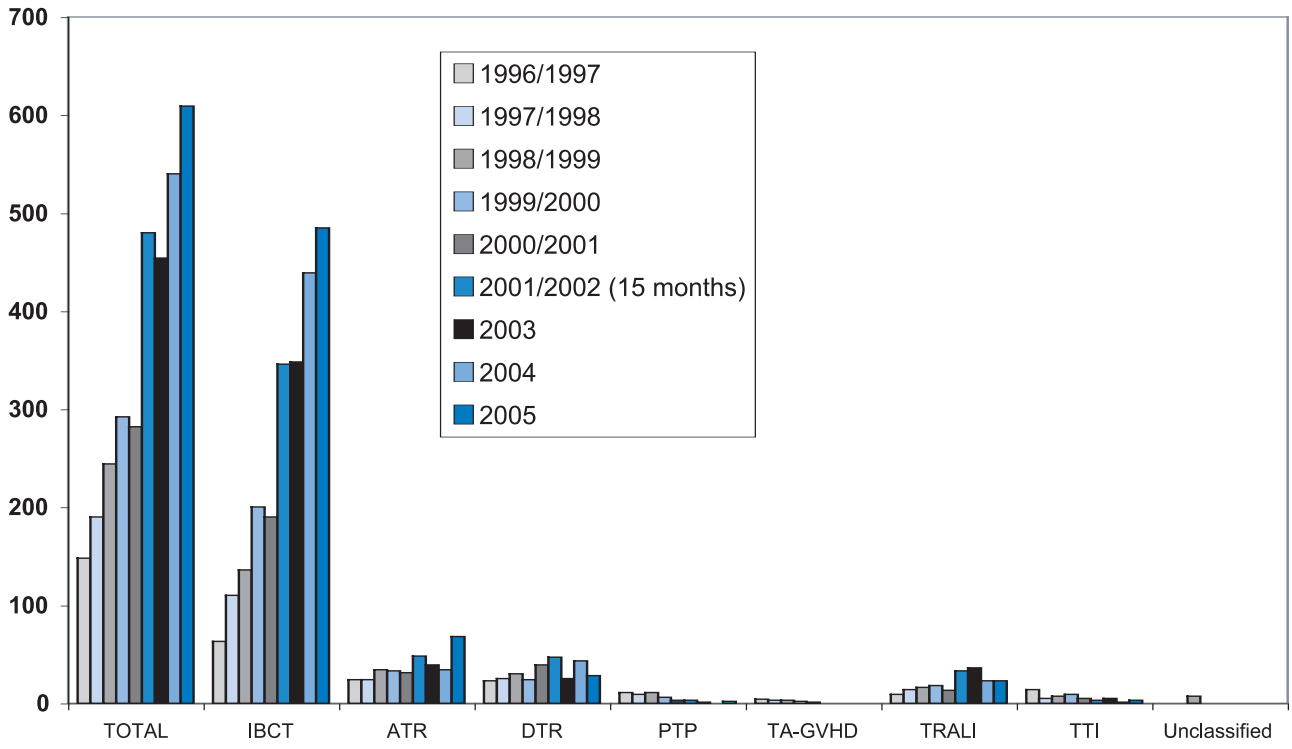


Table 4

Cumulative mortality / morbidity table 1996 - 2005

	Total	IBCT	ATR	DTR	PTP	TA-GvHD	TRALI	TTI
Death definitely attributed to transfusion (imputability 3)	46	7	2	6	1	13	8	9
Death probably attributed to transfusion (imputability 2)	13	3	4	1	0	0	5	0
Death possibly attributed to transfusion (imputability 1)	46	12	7	1	1	0	25	0
Sub total 1	**105**	**22**	**13**	**8**	**2**	**13**	**38**	**9**
Major morbidity* probably or definitely attributed to transfusion reaction (imputability 2/3)	296	94	13	29	13	0	110	37
Minor or no morbidity as a result of transfusion reaction	2816	2190	306	246	31	0	37	6
Sub total 2	**3112**	**2284**	**319**	**275**	**44**	**0**	**147**	**43**
Outcome unknown	15	11	3	1	0	0	0	0
Total**	**3232**	**2317**	**335**	**284**	**46**	**13**	**185**	**52**

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

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

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

5. Incorrect Blood Component Transfused

Definition

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.

524 completed IBCT questionnaires were received.

Thirty-nine reports were withdrawn by the analysts. Thirteen of 39 were 'right blood to right patient' incidents, in which the patient received the intended component despite a serious breach of protocol. These are discussed at the end of this section. A further 26 did not meet the criteria for IBCT, one of these was transferred to the Acute Transfusion Reaction chapter of the report.

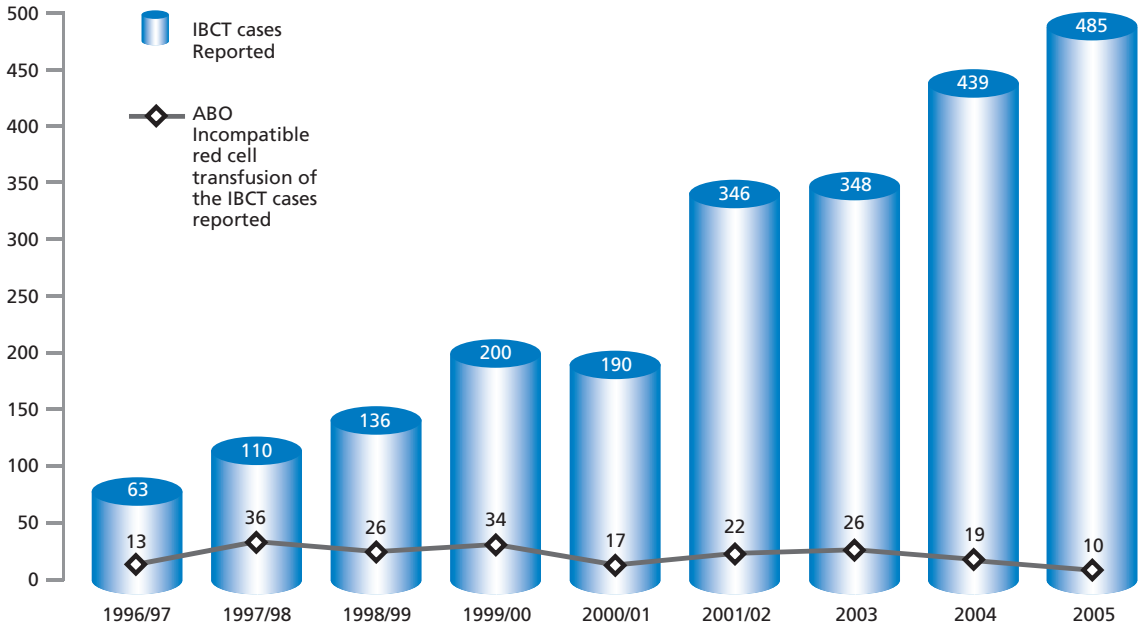
This chapter describes the findings from 485 analysed cases, a 9.3% increase from 2004.

Total numbers of IBCT reports continue to increase, with no sign of a plateau. However the number of 'wrong blood' events, in which there is a risk of a potentially fatal haemolytic transfusion reaction, is the same as in 2004, whilst the number of ABO incompatible red cell transfusions has fallen to 10 (c.f. 19 in 2004).

In figure 6 the blue bars represent the total number of IBCT reports and the black line is the number of ABO incompatible red cell transfusions.

Figure 6

ABO incompatible red cell transfusions



Patients

273 Females

207 Males

5 No data available

Ages ranged from 1 day to 96 years.

Forty-five reports (9%) related to patients under 18 years of whom 25 (5%) were infants under 12 months.

Mortality and morbidity

1 death was due to an ABO incompatible transfusion (Case 1, imputability 3)
1 patient died, possibly related to overtransfusion (Case 17, imputability 1)
1 patient suffered major morbidity due to overtransfusion (Case 18, imputability 2)
1 recipient of an ABO incompatible haemopoietic stem cell transplant received blood of the incorrect group and suffered a severe acute haemolytic reaction

In addition, 2 cases were reported in which misinterpretation of the antibody investigation at antenatal booking resulted in severe haemolytic disease of the fetus, resulting in an intrauterine death in one case and severe morbidity requiring exchange transfusion in another. These cases (Cases 21 and 22) are described in section 7 below.

Analysis of cases

IBCT case reports can be analysed in a number of different ways. This year they are divided into 7 sub-groups, as follows

Type of event	Number (%)
'Wrong blood' events where a patient received a blood component intended for a different patient or of an incorrect group.	87 (18%)
Other pre-transfusion testing errors - including incorrect D groups, missed allo-antibodies and missed serological incompatibility.	22 (4.5%)
Blood of the incorrect group given to recipients of ABO mismatched PBSC or bone marrow transplant.	2 (0.5%)
Failure to provide blood of appropriate specification or that did not meet the patient's special requirements.	141 (29%)
Inappropriate or unnecessary transfusions.	67 (14%)
'Unsafe' transfusions where there were handling or storage errors.	79 (16%)
Events relating to administration of anti-D immunoglobulin.	87 (18%)
Total	**485**

In each sub-group, an attempt has been made to assess the contribution of errors in clinical areas and in laboratories. Because of the increasing emphasis on the importance of good laboratory practice, hospital transfusion laboratory errors, which occurred in 179/485 (37%) of all cases, are summarised in Table 12 at the end of the chapter.

Time and location of transfusion

Previous SHOT Annual Reports have analysed the time and location of transfusion errors, but it has not been possible to draw conclusions from these findings because of lack of denominator data. In September 2005, an observational study on the time and location of blood transfusion was carried out in 28 hospitals in the Northern and Yorkshire regions (H Tinegate, C Thompson, unpublished data).

The fate of all red cell units issued during a 7 day period (n=3118) was recorded, and compared to 169 SHOT reports in which an incorrect blood component was transfused due to an administration error and the time and location was known.

The study found that 888/3118 (28.5%) of red cell units were transfused between 2000 hours and 0800 hours, whereas 63/169 (37%) of blood administration errors took place during this period (p=<0.03). These data support the recommendation that blood should not be transfused at night unless clinically essential.

Transfusions on in-patient wards were associated with excess risk (57.5% of red cells transfused vs 72.2% of errors, p=<0.001), whereas transfusions on day units (12.7% of red cells transfused vs 4.1% of errors, p=<0.001) and intensive care unit (ICU) / high dependency unit (HDU) (13.0% of transfusions vs 5.9% of errors, p=<0.001) were relatively safer.

1 'Wrong blood' events (n=87)

These patients, who received a blood component intended for a different patient or of an incorrect group, could potentially have been at risk of life-threatening haemolytic transfusion reactions.

- Ten patients received ABO incompatible red cell transfusions, 2 of which were also D incompatible.
- Nine patients received ABO incompatible FFP or cryoprecipitate (group O components given to patients of other groups).
- Two patients received ABO incompatible platelets (group O to patients of other groups in error)
- Eight D negative patients inadvertently received D positive cellular components, - none of these was a female of child-bearing age.
- One patient with anti-c received group O rr red cells.
- The remaining 57 patients received components that were fortuitously compatible.

Case 1 - Fatal ABO incompatible transfusion

A 69 year old male with a ruptured abdominal aortic aneurysm was taken to theatre after midnight. The patient's wristband was removed for insertion of an arterial line. A sample had been sent previously to the laboratory for a blood group and antibody screen - the group was recorded as O D positive. Six units of red cells were requested and crossmatched - all were transfused during the operation. A further 4 units were crossmatched and delivered to the satellite blood refrigerator in the theatre suite. When the patient began bleeding again, a nurse was sent for the next 4 units, but instead collected 4 group A D positive units crossmatched for another patient. A staff nurse and a healthcare assistant checked the blood against the compatibility slip. One unit of blood was administered by a consultant anaesthetist and 1 by a specialist registrar (SpR) without a patient identity check. The error was noticed as the 3rd unit was about to be given. The patient suffered an acute haemolytic transfusion reaction, was admitted to ICU for dialysis and ventilation but died 2 days later.

Causes of 'wrong blood' events

Errors occurred at all critical points in the transfusion chain, i.e. patient sampling, laboratory pre-transfusion testing, collection of blood from storage site and administration at the bedside. The site of the primary error, which led to the mistransfusion, is shown in Table 5. This table also illustrates those cases where the primary error could have been detected at a later stage in the chain, but was not. The most common scenario was that the wrong unit of blood was delivered to the clinical area and staff carrying out the pre-transfusion checking procedure failed to detect the error.

Table 5

Site of the primary error that led to mistransfusion

Site of Primary Error	No of cases (%)
CLINICAL (patient sampling)	4 (4.5%)
Also laboratory error	*1*
CLINICAL (wrong blood delivered to clinical area)	23 (26.4%)
Also failure of bedside check	*23*
CLINICAL (blood administered to wrong patient)	23 (26.4%)
LABORATORY	37 (42.5%)
Also failure of bedside check	*4*
Total cases	**87**
Total errors	***115***

Sample errors

Four cases were reported in which the sample for pre-transfusion testing was taken from the wrong patient or labelled with another patient's details. One resulted in an ABO incompatible transfusion. Most such errors can be detected in the transfusion laboratory and are near misses.

Case 2 - Beware patients with the same name!

Fred Bloggs and Joe Bloggs were on the same ward. Neither was previously known to the laboratory. Fred required blood for a revision hip arthroplasty, but the sample was taken from Joe, labelled with Fred's details and grouped as AB D positive. Fred received four units of AB D positive blood; the error was detected when a repeat sample was found to be group O D positive. He suffered no ill effects.

Case 3 - Vigilance needed in the laboratory

A sample for pre-transfusion testing was taken from the wrong patient. The patient's previous record was held on a legacy system but the laboratory staff did not look it up. The blood provided was ABO compatible.

Laboratory errors

In 37/87 (42.5%) of 'wrong blood' reports the originating error occurred in the hospital transfusion laboratory. In one further case (3 above) an error in sampling that could have been picked up by the laboratory was missed due to a previous group being on a legacy system. Twenty-seven errors involved testing and 10 were errors in component selection and labelling.

In 22 cases there was an error in ABO typing. In 9 the wrong sample was selected for testing, in 10 cases there were transcription/recording errors, in 2 cases interpretation errors and in one case the reason for the incorrect result could not be ascertained. Where the wrong sample was selected, manual tests were being performed in 5 cases, in 1 case the wrong sample was labelled before being loaded onto an analyser and in 3 cases the error was unclear. Transcription errors occurred during manual testing in 6 cases and in 4 cases where automation was used without an interface connection. Fifteen of these 22 errors occurred 'out of hours' and 6 occurred during routine working hours, whilst in 1 the time of error was not given. Twelve of the cases were classified as urgent, 6 as routine and in 4 cases the urgency of the test was not given. Three of these 22 patients received ABO incompatible red cell transfusions, and 6 incompatible FFP.

In 9 cases there were component selection errors. Three of these were group O FFP or cryoprecipitate provided for patients of group A or B, one of which was a group B D negative infant who also received D positive platelets. A further 4 D positive components (red cells in 3 cases and platelets in 1) were supplied in error to D negative patients. One report was of issue of platelets to the wrong patient and in another case two human leucocyte antigen (HLA) matched platelets that arrived in the laboratory at the same time were switched and issued to the wrong patients.

The remaining 6 cases include 3 incorrect D types (one where the wrong sample was tested, one recording error and one historic error that could not be investigated), 2 crossmatching errors (incorrect sample used in both cases) and a labelling error.

It is of interest to note that 12 of the 27 laboratory 'testing' errors occurred because the wrong sample was selected for test.

22 of these 37 errors (59%) occurred outside of core hours.

Learning points

- Basic training for biomedical scientists must reiterate careful sample identification at the point of test.
- Robust systems must be in place for recording results of both manual and automated tests if electronic interfaces are not in place.
- Competency based training for laboratory staff must include those working out of hours.
- A laboratory quality system, as required by the Blood Safety and Quality Regulations, must include internal incident reporting mechanisms and appropriate, documented, corrective actions.

Collection and administration errors

In 23 cases the wrong blood was collected from the refrigerator and delivered to the clinical area, and the error was not detected when the blood was administered to the patient. In a further 23 cases, the correct blood was delivered to the clinical area but was given to the wrong patient. Four cases were reported in which a laboratory error might have been detected at the bedside but was not. Thus there were 50 cases where the pre-transfusion checking procedure was carried out incorrectly or omitted altogether.

Seven of these errors resulted in ABO incompatible transfusions - it is notable that in 6 of these the 'checking' of the blood was done using the compatibility form, whilst in the seventh a theatre prescription was used as the patient wristband was inaccessible.

Case 4 - Transfusion errors may affect more than one patient.

'Emergency O D negative' blood was requested for a patient bleeding in theatre. A nurse collected 2 units that were group O D negative but crossmatched and labelled for 2 other patients. One unit was blood of a very rare phenotype - the intended recipient's planned surgery had to be postponed whilst the blood service screened further units.

Case 5 - Safety systems are only effective if correct procedures are followed.

A nurse was asked to set up a transfusion for Jill Archer. She found that Jill was not wearing a special 'red label' transfusion wristband, and the laboratory informed her that no blood had been requested. She informed a doctor who promised to 'sort it out'. Meanwhile blood was delivered to the ward for Kathy Perks, together with some spare 'red label' numbers. The nurse assumed that the blood was for Jill Archer, she attached the labels to a wristband and transfused the blood. A second doctor discovered the error when reviewing Jill Archer and finding that blood had not been prescribed. The blood was compatible.

Learning points

- A final patient identification check must always be carried out before transfusion using the identity band or formally risk assessed alternative attached to the patient.
- Safety systems must be supported by training and education of all staff involved in transfusion, to ensure that correct procedures are followed.
- Routine pre-transfusion testing should not be done outside of core hours unless there are adequate numbers of appropriately skilled staff.
- Administration of blood should only take place at night when clinically essential.
- Procedures must be in place for collection of blood from refrigerators and must include the requirement to check against the patient's minimum identification dataset.

2 Other pre-transfusion testing errors - incorrect D groups, missed alloantibodies and missed incompatibilities (n=22)

Three of these 22 cases involved neonates and 12/22 occurred 'out of hours'.
Cases where antigen negative blood should have been selected for a patient with a known antibody, but was not, are included in the 'Special requirements not met' section.

The 22 errors can be split into procedural errors i.e. incorrect test/component selection (15 cases of which 3 were neonates) and testing errors i.e. the correct tests were performed but incorrect results were obtained (7 cases).

10/22 errors (6/7 testing errors and 4 procedural errors) involved the antibody screen. In 3 of these cases, all neonatal patients, the antibody screen was either not performed when it should have been or maternal results were not looked up. In 3 cases a positive antibody screen was 'missed' due to software problems in automated systems, in 1 case a weakly positive result was modified to negative on an automated system, in 1 case a weak antibody was missed by a manual technique and investigation of the case revealed a pipetting problem, and in 1 case the BMS forgot to read the antibody screen. In one case outdated screening cells were used.

The seventh testing error was a missed anti-A1.

A further 5 procedural errors included 1 case where a repeat antibody identification panel should have been set up and was not, 2 cases where crossmatch compatible blood was issued without selection of appropriate antigen negative units, a case where electronic issue was used when an indirect antiglobulin test (IAT) crossmatch should have been performed and a case in which the laboratory failed to look for a masked allo-antibody in a patient with a positive direct antiglobulin test (DAT), resulting in a haemolytic transfusion reaction.

In 5 cases, laboratories failed to request fresh samples for pre-transfusion testing from recently transfused patients, contravening BCSH guidelines and running the risk of missing a recently developed allo-antibody.

In 1 case a BMS thought that 'high risk' patients need not be tested pre-transfusion and entered negative results for a crossmatch that had not been performed.

A number of cases of laboratory errors appear to show chaotic practices either because laboratories are too busy or because of 'poor housekeeping'.

Case 6

A patient had undergone emergency plastic surgery and was found to have a post-operative Hb 6.5g/dL. Four units of blood were requested. There was no historical transfusion record. The on-call BMS carried out a group and antibody screen, and issued 4 units red cells as compatible by immediate spin cross-match, but failed to read the antibody screen. This was only noticed to be positive when an antibody screen on another patient was read. Anti-E was identified by panel. The BMS phoned the ward to halt the transfusion - the patient had received <50 mL with no adverse sequelae.

Case 7

A crossmatch request was received via A & E for a patient with a fractured neck of femur. The laboratory staff processed the sample on the IBG analyser; results showed a positive antibody screen. As the blood was not required immediately, a decision was made to perform an antibody panel during the next routine day. Later that afternoon, during the on-call period, a request was made for 2 units of blood. A panel was then performed and the results suggested an antibody, but the results were not consistent with those of the antibody screen. This was later found to be due to the fact that the screening cells had been changed in the last 24 hours but the result sheet had not been changed to the new batch - unknown to the on-call member of staff. Six units of blood were put up for crossmatch of which 2 were compatible. In view of the disparity between panel and screen, these 2 units were issued as crossmatch compatible with the appropriate documentation and were not screened for the presence of the suspected antigen.

3 Blood of wrong group given to recipients of ABO mismatched haemopoetic stem cell transplants (n=2)

Recipients of ABO mismatched stem cell transplants require the utmost care in provision of blood components during engraftment.[18] Two cases were reported in 2005 in which patients were given blood components of an incorrect ABO group.

In 1 case the laboratory was not informed that the patient had received a transplant, and only suspected this when discrepant ABO grouping results started to develop. In the second case the laboratory staff did not adhere to the protocol and selected blood of the incorrect group, then compounded the error by incorrectly performing the crossmatch and failing to detect incompatibility. The patient suffered an acute haemolytic transfusion reaction.

4 Failure to provide components of appropriate specification or that did not meet special requirements (n=141)

There was a similar number of cases in this category to last year (143).

These cases are summarised in Table 6.

In this subgroup of cases, errors occurred at all points in the transfusion process and all types of hospital, including specialist centres with a high throughput of patients with special transfusion requirements.

Selection of unsuitable components by laboratory staff is common and, if the wrong product is issued, failures in the clinical process often lead to mistransfusion. The majority of selection errors are made by regular, experienced staff during normal working hours, although on-call staff who do not routinely work in the laboratory may be less likely to consult the historical transfusion record - this finding has clear implications for training and regular reinforcement /audit of standard operating procedures.

Table 6

Special requirements not met

Special requirement	No of cases
Irradiated components	89
CMV negative components	6
Irradiated and CMV negative	16
Antigen negative red cells for patient with known antibody	20
Antigen negative and Irradiated	1
HPA1a/5b negative platelets for NAITP	2
Neonatal red cell transfusion, exchange transfusion	4
Viral inactivated non-UK FFP for a child	1
HLA matched platelets	1
Pre-deposited autologous red cells	1
Total	**141**

Irradiated components

As in previous years, failure to provide irradiated components formed the large majority of cases in this category. One hundred and six patients (c.f. 84 in 2004) were placed at risk of TA-GvHD although no actual cases of TA-GvHD were reported in 2005. There were 58 males and 48 females with a mean age of 49.5 years (range 6 days to 95 years). Between them, these patients received 204 units of red cells and 28 platelet transfusions. The clinical indications for irradiation in these patients are shown in Table 7.

Table 7

Indication for irradiated products

Indication for irradiated components	No of cases
Purine analogue therapy	44
Stem cell transplantation	29
Hodgkin's Disease	17
Di George syndrome	5
Other T-cell immunodeficiency	2
Severe aplastic anaemia/ALG	3
Neonate, previous *in utero* transfusion	1
Miscellaneous	5
Total	**106**

The site of the primary error, which led to the failure to provide irradiated components, is shown in Table 8. This table also illustrates those cases where further significant errors in the transfusion chain occurred and contributed to the transfusion incident (e.g. the primary error may have occurred in the laboratory, but clinical errors in requesting, prescription or bedside checking allowed the component to be transfused).

Table 8

Site of the primary error that led to the failure to provide irradiated components

Site of Primary Error	No of cases (%)
LABORATORY	30 (28%)
(also clinical error)	*27*
CLINICAL	70 (66%)
(also laboratory error)	*9*
ADMINISTRATIVE OR I.T. ERROR	3
(also laboratory or clinical error)	*2*
PHARMACY	1
(also laboratory or clinical error)	*1*
BLOOD SERVICE	2
(also laboratory or clinical error)	*2*
Total cases	**106**

Although laboratory errors are a common cause of failure to administer irradiated products, in almost every case a concomitant clinical error removed an opportunity to prevent the mistransfusion. Sixteen of the 30 cases would have been prevented by a correctly performed final bedside check against the accurately completed prescription sheet. Laboratory errors equally involved failure to check (or correctly interpret) the historical record (16 cases) or failure to notice or action the requirement for irradiated products indicated on the request form (14 cases). Twenty-eight of the 30 laboratory errors (93%) in this category were made by regular transfusion BMS staff during normal working hours.

Clinicians continue to be unaware of the indications for irradiated products in their patients (especially Hodgkin's disease), fail to communicate with the laboratory and make errors in requesting and prescribing. Better communication between clinical teams 'sharing care' for patients is essential. Thirty-seven per cent of the patients who had received purine analogues and 16% of cases involving stem cell transplantation had been treated at another hospital but no record of their special transfusion requirement had been communicated to the local hospital or transfusion laboratory.

This report includes 5 cases of babies or children with Di George syndrome undergoing surgery for congenital heart disease. In 4 cases the clinical team failed to indicate the diagnosis or order irradiated products and 1 case was due to laboratory error.

Errors primarily caused by administrative or IT problems included a patient with duplicate hospital numbers (the *Irradiated Products* flag was only recorded under one of the numbers), an episode caused by implementing a new laboratory computer system which didn't automatically transfer warning 'flags' and a case where a new hospital Patient Administration System led to failure to locate the correct historical record on the laboratory computer (case 8 below). One patient had several volumes of hospital notes but the *Irradiated Products* sticker was only on one of them.

One of the two Blood Centre errors involved emergency issue of non-irradiated red cells to a hospital that routinely uses *only* irradiated cellular blood products. The non-irradiated red cells were 'missed' by both the hospital transfusion laboratory and the clinical area. In the other case, clinical urgency did not allow time to irradiate the red cells before issue.

Twenty-six of the 106 cases (24%) could have been prevented by a properly performed bedside check against the accurately completed prescription. Twenty-one cases (20%) could have been prevented if all hospital laboratories could access a common database.

Many hospitals have a system where the pharmacy informs the transfusion laboratory of all patients prescribed purine analogues. However, in two cases, the information downloads were only carried out monthly and a patient was transfused with irradiated products in the interval between prescription and notification of the transfusion laboratory.

Case 8

A new Patient Administration System generates dates of birth in US format (month/day/year). The laboratory computer cannot search by unique indicators (hospital or NHS number) and historical records are located by entering date of birth, first name and surname. Using the date of birth format from the request form failed to locate the correct patient record that contained an Irradiated Products *flag.*

Cytomegalovirus (CMV) negative components

Sixteen of the 22 cases of failure to transfuse CMV negative components (73%) were also associated with failure to issue irradiated components. Affected patients ranged from 1 day to 82 years of age (mean 35 years). None of these cases was reported to result in CMV transmission.

Ten cases were primarily caused by laboratory errors, 11 were clinical errors and one case resulted from failure of the Blood Centre to issue CMV negative red cells in an extreme emergency. Analysis shows that the root causes of failure were much the same as for irradiated products. Only one case involved the emergency issue of blood components. Regular staff, working during normal hours, made 90% of the laboratory errors. Two cases involved specialist clinical teams being unaware of the local policy, based on consensus advice,[19] for the provision of CMV negative products in patients with HIV infection.

Seven of the cases (32%) could have been prevented by a properly performed bedside check against the accurate prescription.

Antigen negative red cells for patient with known antibody

There were 21 reports in this category, in patients ranging from 2 months to 89 years of age. Nineteen of these cases (90%) were due to laboratory error. Eight involved failure to consult the historical record on the laboratory computer (6 were perpetrated by on-call staff who do not work routinely in the transfusion laboratory and 2 of these were locum staff). In 4 cases laboratory staff, because of incorrect interpretation of results or 'human error', selected an incorrect component. Two cases were communication errors. In one case staff failed to communicate information between shifts and, in the other, incompatible computer systems in two laboratories *in the same Trust* were unable to transfer the historical record between sites. Transcription errors in manually transferring historical data to a new laboratory computer system led to two reports from the same hospital (Cases 9 & 10).

Two cases were due to clinical errors. In one case the ward medical staff failed to contact the laboratory even though the patient produced an antibody warning card from another hospital. In the second case, there was a failure to inform the laboratory when the donor for an allogeneic blood stem cell transplant was changed (Case 11).

Cases 9 and 10

A hospital commissioned a new laboratory computer system. Unfortunately, it was not possible to transfer data electronically from the old system to the new. Manual transcription of the historical record led to two errors. In the first case, a patient with anti-c and anti-E was transcribed as anti-C and anti-E. The second case was altered from anti-Lu(a) and anti-E to anti-Lu(a) and anti-e. This led to the transfusion of 9 units of red cells of the inappropriate groups, but with no significant clinical sequelae.

Case 11

A D positive patient underwent haemopoietic stem cell transplantation from a D positive donor. Unfortunately, the graft failed and the patient underwent a second transplant, this time from a D negative donor. The laboratory was not informed of the second transplant and continued to supply D positive red cells. The immunosuppressed patient received a total of 79 D positive red cell transfusions over a 5 month period without any adverse reactions or becoming sensitised to the D antigen.

Neonatal transfusions

There were 6 incidents involving neonatal transfusions of red cells or platelets outwith the above categories.

In two cases of neonatal alloimmune thrombocytopenia (NAITP) there was a failure to issue HPA1a/5b negative platelets. One case was a combination of poor clinical communication and failure to consult the historical record (the baby had already had intrauterine platelet transfusion). In the second case, HLA-matched platelets for another patient arrived in the same urgent delivery from the blood centre as the HPA1a/5b negative platelets for the baby. There was poor communication between the clinical team and the laboratory and 'HLA-matched platelets' were written on the baby's prescription chart. The HLA-matched platelets were issued and transfused to the baby with no adverse clinical sequelae.

Two neonates needing urgent red cell transfusion were given the emergency O D negative blood intended for adult patients rather than the emergency paediatric pack. In both cases the clinical staff (Special Care Baby Unit and Obstetric Operating Theatre) were unaware of the location of the emergency paediatric blood or the special requirements of their patient.

Failure to issue viral-inactivated non-UK FFP for a child less than 16 years

In 2005 there was only one reported case, compared to 9 in 2004.

Preoperative autologous donation of red cells (PAD)

One case was reported to SHOT in 2005.

Case 12

A 64-year-old woman was scheduled for primary total hip replacement. The orthopaedic surgeon arranged for 2 units of autologous red cells to be collected in the hospital prior to surgery. The laboratory procedure was not to 'reserve' the autologous units on the patient's laboratory computer record until a request for blood was received. When the clinical team requested blood, the on-call biomedical scientist (who did not work regularly in the transfusion laboratory) crossmatched and issued 2 units of allogeneic blood, which were transfused to the patient.

As well as highlighting problems with internal laboratory procedures, communication and clinical checking, this case well illustrates that PAD does not protect patients against the most common serious hazard of transfusion, i.e. transfusion of an incorrect component. The patient's preoperative Hb was only 10.8g/dL after the donations, increasing her risk of needing perioperative transfusion and exposing her to transfusion hazards. Preoperative optimisation of Hb, strict transfusion triggers and use of cell salvage, where appropriate, obviates the need for transfusion in most such cases. 'Routine' use of PAD is no longer supported by the National Blood Transfusion Committee for England and North Wales or the English National Blood Service.

Learning points

- Hospital and laboratory IT systems should use compatible patient ID parameters to ensure that correct historical transfusion records are accessed rapidly and efficiently. Laboratory IT systems should be updated with special requirements and data should be transferred electronically to new systems. Systems should, if possible, be routinely updated with new rules, e.g. methylene blue non-UK FFP for patients under 16.
- Several laboratory errors were caused by failure to notice the *Special Requirements* box on the transfusion request form. The format of transfusion request forms should be reviewed to ensure this section is appropriately prominent. Electronic requesting systems should ensure completion of this section is mandatory. Laboratories should also insist on appropriate clinical details on request forms - 'anaemia' or 'pre-op' is not sufficient.
- Clinicians have a responsibility to be aware of the special transfusion needs of their patients and to ensure that local systems for notifying the laboratory are followed. Hospitals should consider implementing a system of informing the laboratory as soon as the requirement for irradiated components is identified. In the case of purine analogue therapy, routine notification of the transfusion laboratory by the hospital pharmacy is an effective safety measure, although data should be transferred at frequent intervals to prevent patients receiving non-irradiated products in the 'window period'. Where patients have several volumes of hospital notes, each should be 'flagged' with the special transfusion requirements.
- Blood request forms must be accurately completed and transfusion prescriptions must indicate special requirements.
- The final bedside check is the last barrier to mistransfusion and appears to fail in 20 to 40% of cases - research into ways of improving its effectiveness and evaluation of new technologies to improve the process is essential.
- Communication, both between clinicians in specialist treatment centres and local hospitals, and between clinical teams within hospitals, must be improved. Data on special transfusion requirements should be communicated between transfusion laboratories in hospitals that routinely 'share' patients.
- Greater emphasis should be placed on involving patients in ensuring their special transfusion requirements are met. Simply issuing 'Irradiated Component' cards to patients appears to have been of limited benefit. The introduction of a patient held booklet (analogous to the commonly used anticoagulant booklet), together with targeted education, should be considered for patients following stem cell transplantation and purine analogue therapy and would be a suitable area for clinical research and pilot studies.

5 Inappropriate or unnecessary transfusions (n=67)

Reports of these cases, in which patients received blood components unnecessarily, have increased from 56 in 2004. The underlying causes are shown in table 9. SHOT does not currently accept reports of non-compliance with guidelines on appropriate use. Such cases are difficult to assess retrospectively by a third party, and appropriate use of blood is best evaluated by well constructed prospective clinical audit such as the National Blood Service/Royal College of Physicians National Comparative Audit.

However 7 cases are included in which patients were grossly overtransfused, contributing to the death of one patient and major morbidity in another. We plan in future years to include a category of transfusion associated circulatory overload (TACO) and have included these cases in anticipation of this development.

Table 9

Site/stage of primary error leading to inappropriate transfusion

Primary error	Number
Unsuitable sample for FBC, e.g. from 'drip arm or from wrong patient (CLINICAL)	27
Also laboratory error	*6*
Also clinical (request) error	*5*
Analytical error (HAEMATOLOGY LABORATORY)	10
Also clinical (request) error	*2*
Near-patient testing error (CLINICAL)	5
FBC misinterpreted or wrongly transcribed resulting in request error (CLINICAL)	5
Wrong component/product selected (TRANSFUSION LABORATORY)	4
Wrong component collected from hospital transfusion laboratory (CLINICAL)	9
Also failure of pre-transfusion check against prescription	*15*
Overtransfusion due to clinical misjudgement (CLINICAL)	7
Total cases	**67**
Total errors	***95***

The most frequent underlying cause in this sub-category was faulty blood sampling; from a 'drip arm' in 11 cases, settled in a syringe in 3, haemolysed in 1, insufficient in 1. In a further case a sample was taken from a Hickman line, apparently using the correct technique, but was dilute. Two cases resulted from a full blood count (FBC) sample taken from the wrong patient. In the remaining 8 cases the cause of the sample error was not found. In 3 cases the haematology laboratory issued a provisional report and requested a repeat sample, but instead the patient was transfused. In 6 cases the haematology laboratory failed to investigate a large discrepancy between the current and recent result, subsequently found in 4 cases to be due to clots in the sample.

Case 13 - Faulty blood sample and lack of communication results in unnecessary transfusion.

Samples for full blood count and biochemistry were taken from a patient using a syringe, because of difficulties with venous access. The biochemistry laboratory reported that the sample was haemolysed and requested a repeat. The haematology laboratory were not alerted to the potential problem and did not notice the haemolysis. They processed the sample and issued an erroneous report, as a result of which the patient was transfused with 2 units of blood.

Case 14 - Does the clinical picture fit the laboratory report?

A female patient was admitted as an emergency with an intra-uterine death. The full blood count results and coagulation screen suggested a diagnosis of disseminated intravascular coagulation but there were no clinical signs of this complication. The ward queried the results with the laboratory and were reassured that they were genuine. Two units of red cells and 4 units of cryoprecipitate were transfused. The sample was subsequently discovered to contain clots.

A further 15 cases resulted from analytical errors, 5 of which were near-patient testing, including 2 haemoglobin results from blood gas analysers.

Case 15 - Haemoglobin result from blood gas analyser cannot be relied upon.

A collapsed patient was admitted to a coronary care unit. A haemoglobin estimation on a blood gas analyser gave a result of 2g/dL. A sample was sent to the laboratory and in the meantime 2 units of uncrossmatched group O D negative blood were transfused. The haemoglobin result from the laboratory was 10.7g/dL. The patient suffered no ill effects as a result of the transfusion.

In 4 cases, a decision to transfuse was based on a laboratory report that was either misunderstood (in one case a white cell count was mistaken by a junior doctor for a haemoglobin and in one case the red cell distribution width (RDW) was taken to be the platelet count) or wrongly transcribed (in one a mother's FBC result was written in her infant's notes).

Thirteen cases were reported in which there was apparent confusion over which blood component had been recommended and/or prescribed, reflecting a lack of knowledge of the indications, and in some cases the appearance, of components, and a lack of rigour in prescribing and administering blood.

Case 16 - Be careful how you delegate!

A haematology SpR requested platelets from the transfusion laboratory for his patient, and instructed the house officer to 'write them up'. The house officer asked a nurse how to prescribe platelets and was advised to write '2 bags FFP over 30 mins'. A different nurse, on seeing the prescription, telephoned the laboratory to request FFP, which was provided and transfused. The SpR discovered the error on finding the labelled platelets still on the agitator next morning

Learning points

- All staff undertaking phlebotomy must understand the importance of correct patient identification and correct sampling technique, and must be assessed as competent.
- Blood should only be prescribed by a doctor who has undergone training in blood transfusion and has been assessed as competent.
- Diagnostic laboratories must carry out checks to identify large changes in parameters ('delta checks') and should communicate discrepancies to other laboratories.
- Near patient testing must be subject to the same standards of validation and quality assurance as the diagnostic laboratory.

Seven reported cases of overtransfusion illustrated the difficulty of evaluating acutely bleeding patients and the importance of clinical and laboratory monitoring.

In 6 of these cases, blood loss was over-estimated and too much blood was given, contributing to one death (case 17) and one case of major morbidity (case 18). The pitfalls of blood administration to infants are illustrated by case 19.

Case 17 - wrong diagnosis leads to inappropriate transfusion.

A 62 year old female patient was admitted in a collapsed state with abdominal distension and thought to have a ruptured abdominal aortic aneurysm. A Hb result on a blood gas analyser was 15g/dL. Notwithstanding, the patient was transfused with 3 units of 'emergency O D negative' blood; the post-transfusion Hb was 18.6g/dL. She developed cardiac failure and subsequently died. The presumptive diagnosis of ruptured abdominal aortic aneurysm was not confirmed and the cause of death was uncertain.

Case 18 - importance of regular monitoring in acute bleeding.

A patient with gastro-intestinal bleeding was admitted with a Hb of 6.3g/dL. Four units of blood were prescribed. During transfusion of the third unit the patient was noted to be pale and was continuing to bleed. A further 6 units of blood were given without any interim monitoring. Following transfusion of all 10 units, the patient had a Hb of 19.6g/dL and had developed severe circulatory overload.

Case 19 - Transfusion to infants needs careful monitoring.

During a surgical procedure on a 3 month old infant, the anaesthetist was administering blood via a 3-way tap. He 'lost count' of the volume of blood transfused and the post-operative haemoglobin level was 20g/dL. The infant was venesected and survived without ill-effect.

6 'Unsafe' transfusions (n=79)

Seventy-nine patients (c.f. 54 last year) received potentially 'unsafe' transfusions - details are given in Table 10. Although these cases of handling errors are relatively low risk, the increase in reporting reflects improved vigilance and awareness of the importance of maintaining integrity of the 'cold chain' in hospital, and of adherence to national guidelines (BCSH and Handbook of Transfusion Medicine)[20],[12] on blood component handling and administration. These cases have not been analysed according to laboratory or clinical responsibility, as in many cases responsibilities for satellite refrigerators were not clearly assigned.

There was no resulting mortality or serious morbidity.

Table 10

Type of error	Number
Blood out of temperature control	43[1]
Blood component given was past its expiry or suitability date	24[2]
Blood components transfused over an excessive time period	9[3]
Other	3[4]
Total errors	**79**

[1] ***Blood out of temperature control (n=43)***

In 3 of these cases the transfusion was also prolonged.
13 cases related to the same incident, in which there was failure of a satellite refrigerator in a clinical area, the refrigerator was taken out of use and was clearly marked, but ward staff continued to remove blood from the main blood issue refrigerator and store it in the failed refrigerator.
In another incident, a satellite refrigerator in a theatre suite failed, the alarm sounded, and theatre staff re-set the temperature in order to silence the alarm.
In 2 cases an electronic tracking system was over-ridden.
In 2 cases blood was stored in a ward drug refrigerator, and in 1 case in a satellite blood refrigerator that was not yet commissioned.
Five reports related to the same incident, in which a cold room failure occurred following a planned electrical shut-down at a weekend. The laboratory was unattended and the remote alarm did not sound.
Two cases related to failure of a hospital transfusion laboratory refrigerator and also of the alarm.
Two cases related to units of blood that were left in a satellite refrigerator during cleaning by a medical laboratory assistant. The temperature in the refrigerator was later noted to be outside acceptable levels during and for several hours after cleaning.
In one case blood was out of temperature control during transit with a patient between hospitals. The laboratory at the receiving hospital accepted it into stock and subsequently issued it.
In 1 case FFP had been out of temperature control in transit from the blood centre. The receiving hospital was not informed until 17 days later, by which time 3 patients had been transfused.
In one case thawed FFP was held on a ward at room temperature for over 4 hours prior to transfusion.
In 12 cases red cells were in uncontrolled conditions in clinical areas for >30 minutes, before either being transfused over a period of >4 hours or returned to stock and subsequently re-issued and transfused.

[2] ***Blood given past its expiry or suitability date (n=24)***

In 2 cases the blood was also out of temperature control prior to transfusion, in one of which the transfusion was prolonged.
In 8 cases there was a failure of stock control by the laboratory, followed in all 8 cases by failure to note the expiry date when the blood was given. One of these was a neonate in extremis, - O D negative blood was taken from the emergency stock and transfused, 2 days past expiry.
In 5 cases blood components were issued close to expiry, and clearly labelled, but transfusion was delayed. In one of these cases an electronic system was by-passed.
In 9 cases the 'crossmatch expiry' was marked on the compatibility label but was not adhered to by clinical staff giving the blood. One of these units was also past its expiry date.

[3] ***Blood components transfused over an excessive time period. (n=9)***

UK guidance[12] recommends that:

- From starting the infusion of red cells (puncturing the pack with the infusion set) to completion, infusion of the pack should take a maximum of 4 hours
- Platelets should be infused over not more than 30 minutes
- Infusion of FFP should be completed within 4 hours

[4] ***Others. (n=3)***

In one a gelatinous precipitate was present in solvent detergent FFP (SD-FFP), and in another an unsuitable giving set was used.
Case 20 showed a lack of understanding by nursing and laboratory staff of correct procedures for handling blood components.

Case 20

Two units of FFP were requested and thawed, but were not labelled. They were collected from the laboratory by a porter and delivered to ICU. Two nurses 'checked' the FFP and set up the first unit. The BMS then discovered the labels on the bench and recalled the FFP. The first unit was taken down, a spigot was inserted and it was returned to the laboratory. The BMS attached the labels and returned the FFP to the ICU where the transfusion was re-commenced.

Learning points

- The need for every satellite refrigerator should be carefully risk assessed and reviewed regularly. Clear protocols establishing the responsibilities of the laboratory and nursing staff must be implemented.
- Transfusion laboratory stock control procedures should ensure that expired units are cleared from issue locations.
- Nurses giving blood must be familiar with current guidelines on the handling of blood components.
- Competency training for ward staff must reiterate the requirement for red cells to ONLY be stored in monitored blood refrigerators and must highlight the differences between a blood refrigerator and a normal ward refrigerator.
- Pre-transfusion checking procedures must include checking of the expiry date of the component and noting any end-date for suitability provided by the laboratory.

7 Adverse events relating to anti-D immunoglobulin (Ig) (n=87)

Eighty-seven events were related to anti-D immunoglobulin administration (c.f. 67 in 2004) and are summarised in table 11 below.

Table 11

Primary errors in cases involving anti-D Ig administration

Type of event	Number
Omission or late administration of anti-D Ig Clinical error in 20 (7/15 in community) Laboratory error in 7 (2 also clinical errors)	27
Anti-D Ig given to D positive patient All clinical errors (7/23 in community, 2 also laboratory error)	23
Anti-D Ig given to patient with immune anti-D Clinical error in 4 (2/4 in community) Laboratory error in 3 (1 also clinical error)	7
Anti-D Ig given to patient with weak D antigen [1] All laboratory errors	6
Anti-D Ig given to mother of D negative infant Laboratory error in 4 (1 also clinical error) Clinical error in 3	7
Anti-D Ig given to wrong patient All clinical errors in hospitals	6
Expired anti-D Ig given All clinical errors (8/9 in community)	9
Other[2] (1 in laboratory, 1 clinical error)	2
Total cases	**87**
Total errors	***93***

[1] These events should probably be regarded as limitations of available technology and not errors.

[2] One patient given 10 x correct dose issued by laboratory, 1 given IV preparation because of incorrect ward protocol.

For the first time, cases were reported in which misinterpretation of the antibody investigation at booking resulted in severe haemolytic disease of the fetus, resulting in an intrauterine death in one case (case 21) and severe morbidity requiring exchange transfusion in another (case 22). In a further case (case 23) no routine antenatal serology was done. This case has not been included in the numerical analysis as it does not fulfil the criteria for IBCT.

Case 21

Anti-D was detected at booking and a repeat sample requested by the laboratory. This was not sent; the GP interpreted the results as normal, and entered the patient on the routine antenatal anti-D prophylaxis (RAADP) programme. The reference laboratory did quantitation on the 28 week sample and found the anti-D level to be 141iu/mL. They alerted the Fetal Medicine Unit who attempted to contact the GP, but in the meantime the patient was admitted with an intrauterine death.

Case 22

Anti-D was detected at booking but assumed by the laboratory to be due to prophylactic anti-D Ig given to cover amniocentesis. No quantification or follow-up was carried out. In fact the patient had been found to have immune anti-D in 1994, but the laboratory computer records prior to 1995 were not accessible and the clinical staff had not looked up the notes of the previous pregnancy. No quantification was done during pregnancy - at delivery the infant had severe haemolytic disease of the newborn (HDN) and required exchange transfusion.

Case 23 (not included in numbers)

A patient delivered an infant with severe HDN. No samples had been taken during pregnancy. A historic group O D negative was recorded in the notes.

Learning points

- Training and competency assessment of BMSs in antenatal serology testing and the indications for issue of anti-D Ig must be comprehensive.
- There is an urgent need for education of primary care staff in the basic principles of antenatal serology and current relevant guidelines.

Table 12

Summary of blood transfusion laboratory errors - all cases (where known)

	Total Errors	Wrong Sample	Transcription	Interpretation	Component Selection Errors	Labelling	Procedural Errors	Incorrect Protocol	Testing	Not known
'Wrong Blood' - ABO group	22	9	10	2						1
'Wrong Blood' - Others	15	3	1		9	1				1
ABO mismatched transplant	1						1			
Special Requirements Not Met	72				72					
Inappropriate Transfusion	4				4					
Anti-D Errors	23	1	3				13	1	5	
Unsafe Tx	20						20			
Other Pre-tx Testing Errors	22						15		7	
Total errors	**179**	**13**	**14**	**2**	**85**	**1**	**49**	**1**	**12**	**2**

'Right blood to right patient' (RBRP) (n=67)

As in previous years, we have given reporters the opportunity to report incidents where the right blood was transfused to the right patient despite one or more errors which should have led to the unit being rejected. These incidents do not fit the definition for IBCT but are, nevertheless, instructive. They are not included in the overall numbers of IBCT.

The 67 cases are summarised in table 13.

Table 13
Right blood to right patient episodes

Elements which were wrong on blood packs, documentation, identity bands etc.	Number of incidents
DOB alone or with other elements	22
Name alone or with other elements	16
Hospital or NHS number	11
Transposed labels on 2 units	7
Units unlabelled	3
Hospital transfusion lab records not signed on collection	3
Miscellaneous:	
2 labels on 1 unit	1
Address only	1
Platelets issued retrospectively	1
DOB missing completely	1
1 unit given without prescription	1

Regardless of what the error was or where it was made or by whom, the vast majority of these transfusions (90%) should have been prevented by one or more checking procedures.

Table 14 shows where the error(s) should have been picked up but were not or were ignored.

Table 14

The checking procedure(s) which failed to identify the error(s)

Checking procedure	Number of incidents
Bedside checking	40
Clinical decision to proceed	5
Laboratory + collection + bedside checking	4
Laboratory	3
Sampling and bedside checking	2
Laboratory + bedside checking	2
Collection	1
Collection + bedside checking	1
Blood centre + laboratory + bedside checking	1

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

RBRP case 48

A sample from a premature baby was taken and labelled as 'Baby Girl' instead of 'Baby Boy'. This was noticed by the doctor who took the decision to proceed despite the non-urgent situation. Mis-labelling in the case of neonates is particularly hazardous until the child has been given a full name.

Incidents in which patients are transfused with units labelled with completely the wrong details often involve such a gross failure of the checking procedure that it is difficult to imagine how this can have happened. On the other hand, 'right blood to right patient' incidents illustrate how vital it is to carry out the bedside check in minute detail. It is quite possible that 2 patients on the same ward may have almost identical details which may perhaps differ only by a variation in the spelling of one of their names. Small differences in spelling may be easy to miss but still have the potential for disaster.

RBRP case 60

A misspelt surname on a request form from a hospital to a blood service laboratory went unnoticed by the Blood Centre, who issued a report form and unit labels with the same misspelling. This error was not picked up by the hospital laboratory, nor at collection or at the bedside. The error was eventually noticed at the bedside check for a second unit.

Learning points

- Clinicians should be aware of the potential dangers of transfusing patients when the checking process has highlighted a discrepancy in available information. If the situation is not an emergency it must be standard policy not to transfuse and to begin the process again.
- Staff carrying out the bedside check must check all details in minute detail since a discrepancy in only one letter or digit is potentially dangerous.

COMMENTARY

Notable findings this year were

- There has been a further encouraging reduction in ABO incompatible transfusions, but patient mis-identification continues to cause 'wrong blood' events. The NPSA Safer Practice Notices on wristbands[5] and 'Right patient-right blood'[4] are welcome initiatives.
- Comparison of SHOT reports with denominator data indicates an excess of errors at night.
- Hospital transfusion laboratory errors occurred in 37% of all IBCT cases, an increase from previous years.
- Reports of failure to provide blood of the correct specification for the patient are increasing.
- The reported infant mortality and morbidity due to haemolytic disease of the newborn as a result of misinterpretation of antenatal serology is of major concern.
- In 6 of the 7 reports of ABO incompatible transfusion due to administration error, the pre-transfusion check was carried out away from the bedside using the compatibility form.

RECOMMENDATIONS

The first four recommendations relating to these findings are incorporated in the main recommendations and appear in the Summary. They are repeated here for completeness.

- **Avoid blood transfusions outside of core hours:** Blood administration and pre-transfusion testing outside of core hours have been shown to be less safe and should be avoided unless clinically essential. Hospitals planning to move to 24/7 working must ensure that adequate numbers of appropriately skilled clinical and laboratory staff are available to ensure transfusion safety. It may be useful to audit the occurrence of patient safety incidents in hospitals during different time periods.

  Action: Hospital CEOs, consultant haematologists with responsibility for transfusion together with HTCs and HTTs.

- **Better laboratory practice:** An initiative aimed at improving practice in hospital transfusion laboratories is under way, led by the professional bodies. In the meantime, local quality improvements must be supported and resources provided to underpin the development of quality systems. It is essential that the quality and responsiveness of hospital transfusion laboratories is maintained as Pathology Services in England face major reorganisation following the Carter Report,[11] with the possible development of independent Pathology Trusts and diversification of providers of pathology services.

  Action: Hospital CEOs.

- **Communication of complex transfusion requirements:** Effective mechanisms must be developed for communication of information on complex transfusion requirements (e.g. for patients requiring irradiated components, those with allo-antibodies, stem-cell transplant recipients). Patient awareness and empowerment should be encouraged. Organisations should work together to implement and where necessary develop appropriate tools (e.g. documentation for patients transferred between hospitals, patient held booklets, standard antibody cards with accompanying advice).

  Action: UK National and Regional Blood Transfusion Committees to facilitate and co-ordinate, Hospital CEOs to implement.

- **Improve safety of routine antenatal anti-D prophylaxis:** Implementation of routine antenatal anti-D prophylaxis[15] must be supported by education of primary care clinicians and hospital laboratory staff. Current legislation[16] does not permit issue of anti-D Ig from the laboratory without a clinical request. National guidelines[17] on antenatal testing must be incorporated into agreed local policies and subject to clinical audit.

  Action: Royal Colleges of Midwives, General Practitioners, Obstetricians and Gynaecologists, Consultant haematologists, HTCs and HTTs.

- Hospital transfusion teams should review their system for blood issue and consider whether the compatibility form can be withdrawn.

  Action: Consultant haematologists with responsibility for transfusion.

6 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.

During 2005, 1358 appropriate near miss incidents were reported to SHOT. This is an increase of 26% on the 1076 reported in 2004.

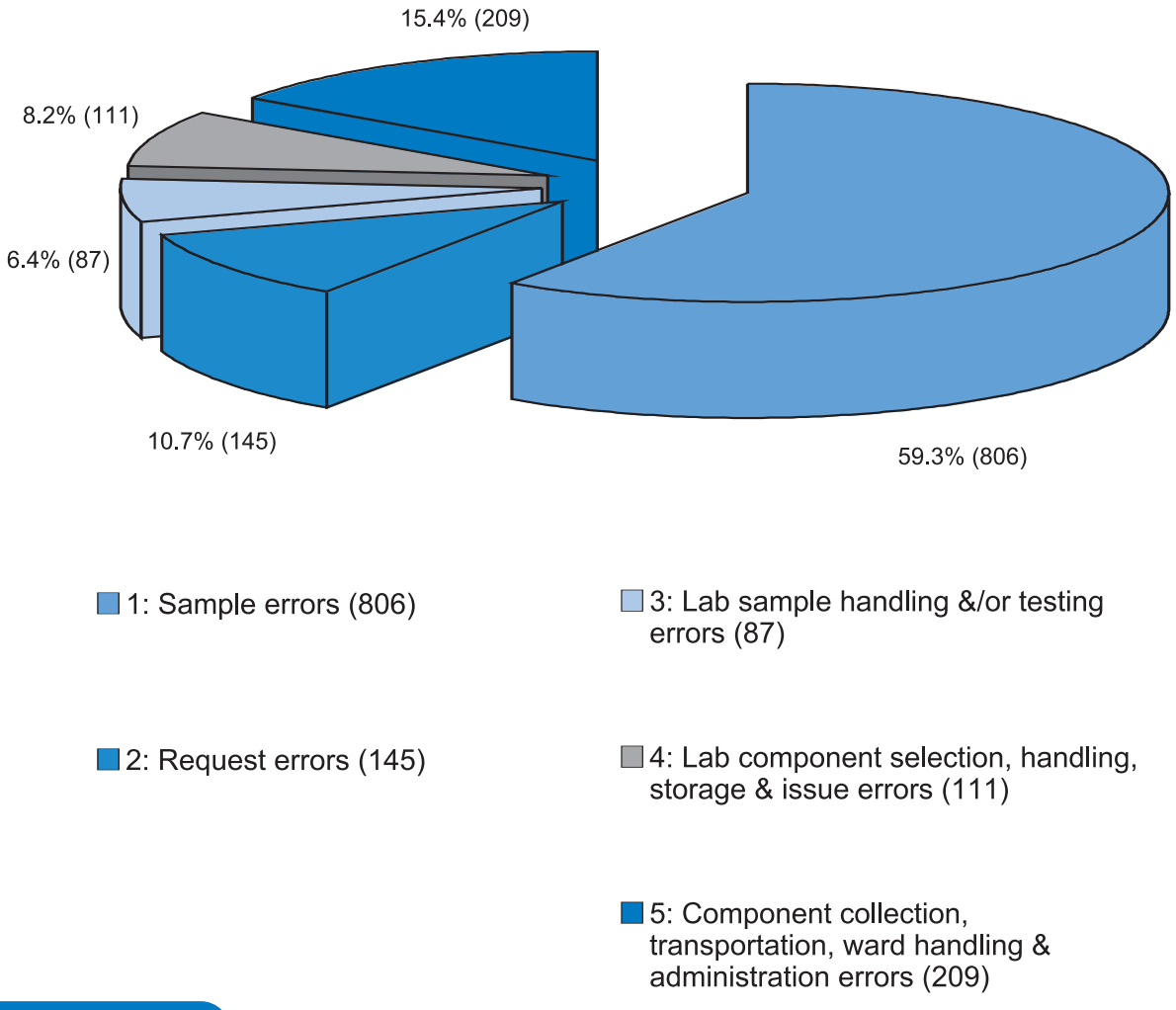
In addition to the incidents submitted on the near miss questionnaires, 3 hospitals sent 'bulk' reports. These figures were collected over a 3 (2 hospitals) and 5 (1 hospital) month period and totalled 204. Of these, 27 reports were not SHOT reportable as they involved unlabelled or no sample being received by the laboratory. As no specific details were provided for the 'bulk' reports, these incidents are not included in the totals.

One incident was written off as the reporter failed to return the completed questionnaire within 6 months and 95 incidents were withdrawn from the analysis. Of the 95 incidents withdrawn, 22 were recategorised as incorrect blood component transfused (including 4 involving anti D administration) and 6 were right blood to right patient events. In 10 incidents the reporter did not have sufficient information available in order to complete the questionnaire and 13 incidents were reported twice. Forty-four incidents were withdrawn as they did not fulfil the criteria for near miss.

The categories and numbers of incidents reported during 2005 are shown in figure 7.

Figure 7

Categories and proportions of near miss events (n=1358)



Category 1: Sample errors (806 cases)

Sample errors were again the most frequently reported near miss events, comprising 59.3% of all incidents. There were 328/1358 cases (24.1% of errors) where the sample was taken from the intended patient but labelled with another patient's details and in 245/1358 (18.0% of errors) cases the sample was taken from the wrong patient but labelled with the intended patient's details.
Errors in the 'Other' category at the sampling stage accounted for 233/1358 (17.2% of errors). The majority of these cases involved samples which were not fully labelled or had one or more identifiers which belonged to another patient.

Category 2: Request errors (145 cases)

Approximately 10% (145/1358) of incidents reported were errors at the request stage. There were 48 (3.5% of errors) cases of components requested for the wrong patient and 45 (3.3% of errors) cases where special requirements were not specified or were specified incorrectly. The majority of request errors were prevented from going on to be full incidents by the vigilance of the laboratory staff.

Category 3: Laboratory sample handling and/or testing errors (87 cases)

This category comprised approximately 6% (87/1358) of errors reported. There were 24 (1.8% of errors) cases which involved mistakes in transcription and 21 cases where an erroneous result was obtained or a result was misinterpreted. More than 50% of laboratory sample handling and/or testing errors were detected by the laboratory staff either by comparison with the patient's historical record or another laboratory check which was performed before releasing the component.

Category 4: Laboratory component selection, handling, storage and issue errors (111 cases)

Approximately 8% of errors occurred in this category. There were 43 incidents involving an avoidable failure by the laboratory to provide for the patient's special requirements. These errors occurred due to laboratory staff failing to act on details in the patient's historical record or on the request form. Forty- seven percent of errors which fell into this category were detected by the ward staff whilst performing the bedside check.

Category 5: Component collection, transportation, ward handling and administration errors (209 cases)

These errors comprised approximately 15% of cases. The majority of the errors occurred at the component handling or storage stage, 130 of the 209 cases. In 54 of these cases the components were not kept in a temperature controlled environment and in 14 cases the components were stored inappropriately, for example platelets being refrigerated. Thirty-five cases involved components which were stored in ward refrigerators. In 2 of these cases, the components were later returned to stock in the transfusion laboratory and in 10 cases the components were available for transfusion after expiry. There were 39 cases where components were collected for the wrong patient, porters were involved in 19 of these.

Table 15 shows the originating errors and at what stage of the transfusion process the error occurred.

Table 15

Originating errors (n=1358)

Originating error	No. of errors	% of errors
Sample error - 806 (59.3%)		
Sample taken from wrong patient but labelled as per intended patient	245	18.0
Sample taken from intended patient but labelled as per another patient	328	24.1
Other	233	17.2
Request error - 145 (10.7%)		
Wrong component requested	19	1.4
Special requirements incorrectly specified which were not previously known to the lab	45	3.3
Product requested for wrong patient	48	3.5
Other	33	2.4
Lab sample handling &/or testing errors - 87 (6.4%)		
Incorrect patient details used	5	0.4
Erroneous result obtained	11	0.8
Result interpretation error	10	0.7
Transcription error	24	1.8
Other	37	2.7
Lab component selection, handling, storage & issue errors - 111 (8.2%)		
Avoidable failure by the laboratory to provide for the patient's special needs	43	3.2
Incorrect selection of component e.g. expired or wrong type of unit	25	1.8
Incorrect labelling of component	27	2.0
Incorrect storage of component	4	0.3
Component issued for wrong patient	4	0.3
Other	8	0.6
Component collection, transportation, ward handling & administration errors - 209 (15.4%)		
Incorrect transportation of component	15	1.1
Component collected for wrong patient	39	2.9
Incorrect handling/storage of component	130	9.6
Error in identification of correct patient at administration	3	0.2
Other	22	1.6

Staff involved in near miss incidents

One thousand two hundred and sixty reports gave information about who was involved in the error, 96 reporters were unable to identify staff involved and 2 reporters gave no response to this question.

The distribution of the staff involved is shown in table 16.

Table 16

Breakdown of staff involved in incidents (n=1358)

Staff group	Sample error	Request error	Laboratory sample handling &/or testing error	Laboratory component selection, handling, storage & issue error	Component collection, transportation, ward handling & administration error
Medical student	1	0	0	0	0
Consultant	4	8	0	0	1
Training grade doctor*	376	74	0	0	6
Non consultant grade^	11	2	0	0	0
Anaesthetist	3	2	0	0	2
G.P.	1	0	0	0	0
Doctor - unkown grade	62	23	0	0	1
Registered nurse	146	15	0	2	71
Midwife	79	17	0	0	30
Phlebotomist	44	3	0	0	0
State registered BMS	0	0	73	94	2
Unregistered nurse	1	0	0	0	5
MLA	0	0	3	4	0
Trainee BMS	0	0	7	2	1
Porter	0	0	0	0	35
BTS staff	1	0	0	8	1
ODA	1	0	0	0	9
Other	13	0	4	0	12
Unknown	62	1	0	1	32
No response	1	0	0	0	1

* e.g. house officer, registrar
^ e.g. staff grade, associate specialists

Of the 806 sample errors reported, 57% (457/1358) involved medical staff compared to 49% in 2004. At the start of 2005 the near miss questionnaire was amended in order to collect information about who performed the phlebotomy in order to assess more accurately which group of staff were responsible for errors at the sampling stage. Medical staff still appear to be making the majority of these errors, however it is still not clear whether this figure is accurate.

Learning point

- All staff groups undertaking venepuncture for pre-transfusion testing should receive education and training and their competency should be tested.

How errors were detected

Approximately 40% (504/1358) of the errors were detected by comparison with computer records, which demonstrates that historical records are a useful tool in the prevention of incorrect blood transfusions. One hundred and fifty one (11%) errors were detected during the bedside check, in 111 cases the check was performed by 2 people, in 28 cases by 1 person and in the remaining 12 cases the reporter could not confirm if 1 or 2 people were involved.

The future of near miss

The number of near miss reports received increased again in 2005, and participation in the scheme has risen to 55% (223/403 eligible hospitals). In order to gain a clearer picture of the number and types of near miss events that are occurring, the collection of individual near miss events was suspended at the start of 2006. The reporting of near miss events to MHRA under the terms of the EU Directive remains unchanged. During 2006 a 6 month survey (June - December) will collect summary information relating to the number of events at each of the following stages of the transfusion process; sampling, request, laboratory testing and issue and collection and administration.

COMMENTARY

- Errors at the sampling stage continue to comprise over 50% of the near miss incidents reported. As in 2004, the data suggests that medical staff were involved in 57% of these errors and again highlights the need for inclusion of education in blood safety in the medical curriculum at undergraduate and postgraduate levels.

- Approximately 10% of errors reported occurred at the request stage. The majority of these were detected by the vigilance of the laboratory staff.

- Laboratory staff failed to provide for the patients special requirements in 39% of the cases in the laboratory component selection, handling, storage and issue errors category.

- There were 209 cases which fell in to the component collection, transportation, ward handling and administration errors category, of these 130 (62%) involved components which were inappropriately handled or stored.

- Since near miss reporting began 5 years ago, the number of reports submitted have increased by 200%. However, only 55% of hospitals are regularly participating in the scheme.

RECOMMENDATIONS

- Training and education in blood sampling, including positive patient ID, should be included in the curriculum for all staff involved in venepuncture.
  Action: Chief Medical Officers (CMOs) NBTC and counterparts, Undergraduate Deans of Schools of Nursing and Medicine.

- All staff involved in the pre-transfusion sampling, testing and issue of blood must be deemed competent having undergone appropriate training, which must be documented.
  Action: Trust CEOs through risk management structures.

- Ward staff at all levels must be trained in appropriate storage of blood components once they have been collected from the transfusion laboratory.
  Action: Ward managers, HTTs.

7 Acute Transfusion Reactions

Definition

Acute transfusion reactions are defined in this report as those occurring at any time up to 24 hours following a transfusion of blood or components, excluding cases of acute reactions due to incorrect component being transfused as these are covered in Section 4

Eighty-nine completed questionnaires were analysed. Twenty-one were withdrawn by the analyst; 15 of these were reports of non-haemolytic febrile reactions, one of which occurred following the re-infusion of red cells salvaged post-operatively, in 5 the symptoms were due to the underlying pathology and the final report withdrawn was of an unavoidable incompatible transfusion that did not lead to a reaction.

This chapter highlights the main findings from 68 completed questionnaires.

Gender (68 reports)

Males 35 Females 33

Age (68 reports)

Age range	6 months to 84 years
Median	56 years

Components implicated (68 reports)

Red cells	23
Platelets	20 (8 apheresis units and 12 from pooled buffy coats)
Granulocytes	1
Fresh frozen plasma (FFP)	22
FFP - solvent-detergent	1
Red cells and FFP	1

Deaths and major morbidity

There was 1 death in this group, likely to be related to transfusion (imputability level 2) and 7 reports of major morbidity; 6 likely to be related (imputability level 2) and 1 possibly related (imputability level 1) to transfusion.

Table 17

Deaths and major morbidity

Outcome	Imputability level	Case number	Component	Reaction type	Comment
Death	2	10	FFP	Anaphylactic/ anaphylactoid	Obstructive jaundice. Vit K not given
Major morbidity	2	6	Red cells	Anaphylactic/ anaphylactoid	Cardiac arrest, severely atopic recipient
	2	8	Red cells	Unclassifiable	Hypoxia requiring ventilation
	2	11	FFP	Anaphylactic/ anaphylactoid	Cardiac arrest
	2	12	FFP	Anaphylactic/ anaphylactoid	Myocardial infarct
	2	13	Platelets	Unclassifiable	Respiratory arrest
	2	14	Granulocytes from family member	Anaphylactic/ anaphylactoid	Ventricular tachycardia
	1	9	Red cells	ALI	Multiple factors

Reactions in which red cells were implicated

There were 23 cases, with 3 instances of major morbidity; 2 likely to be due to the transfusion and 1 possibly due to the transfusion. 17 reactions occurred during the transfusion, 3 within 2 hours, 1 within 7 hours and 1 within 24 hours of completing the transfusion. In the final case the precise timing was unclear.

The following reactions were seen:

Table 18

Reactions in which red cells were implicated

Reaction type	Number of cases
Haemolytic	5
Anaphylactic+	5
Allergic++	8
Unclassifiable	2
Febrile	3 (of 14 initially reported)

+ anaphylactic/anaphylactoid (hypotension with 1 or more of: rash, dyspnoea, angioedema)
++ allergic (1 or more of: rash, dyspnoea or angioedema **without** hypotension)

Haemolytic Reactions

In 3 of the 5 cases, a reference laboratory was involved in either providing antigen matched units or the subsequent investigation of the reaction.

Case 1

A case of a 69 year old lady with a transfusion-dependent myeloproliferative disorder and multiple red cell alloantibodies (anti-K+Kp^a+S+C+Fy^a+Kn^a/McC^a) who had experienced a delayed transfusion reaction to a previous transfusion (see case 13 in the Delayed Transfusion Reaction Chapter). She developed an anti-M over this period but the red cells causing the acute reaction were M-negative.

Case 2

A 65 year old male with gastrointestinal (GI) bleeding had been transfused with red cells within the previous 14 days. A sample less than 48 hours old was used to crossmatch 2 further units. The patient developed a fever and back pain at some stage within the 24 hours following the transfusion. This was not documented contemporaneously, and the nursing staff were unaware of a reaction having occurred. There was however no post-transfusion increment in haemoglobin and brown plasma was noted in the sample sent to the laboratory 36 hours later. The pre-transfusion antibody screen was negative using plasma (DiaMed). Post-transfusion, anti-Jk^a was found in the plasma and eluted from the red cells. Retrospective testing of a pre-transfusion serum sample showed weak reactions with no demonstrable specificity.

Case 3

A 33 year old female, with unexplained red cell aplasia, required monthly red cell transfusions and she had been previously noted to pass dark red urine in the 24 hours following transfusion. On this occasion a poor haemoglobin increment and hyperbilirubinaemia were also noted. The DAT was positive (C3d only), her antibody screen was consistently negative using DiaMed ID and there was no evidence of paroxysmal nocturnal haemoglobinuria (PNH). The reference laboratory found an auto anti-c reacting by DiaMed enzyme IAT.

Subsequent transfusions of R_1R_1 cells have been given with no adverse effects.

Case 4

A 72 year old lady with disseminated carcinoma of the ovary and a previous carcinoma of the breast was transfused in a community hospital with 2 units of red cells. Within 2 hours of completing the second unit, she became febrile and passed dark urine. She was known to have been transfused in 1999 but there was no record of subsequent transfusions. Her pre-transfusion antibody screen using Immucor Capture-R was negative, as were 4 previous antibody screens dating back to 1999. The units had been issued electronically.

The laboratory was only informed of the reaction 10 days later and the post-transfusion sample revealed an anti-K reacting weakly in DiaMed IAT. Further investigation confirmed that the first unit given was K positive.

Case 5

A 45 year old male with HIV, anaemia and a positive DAT (IgG and C3d), being treated with antiretroviral therapy was transfused with 2 units of red cells. The patient was not known to have autoimmune haemolysis (rare in this condition although a positive DAT is common). After receiving 100mL of the second unit, he developed rigors, back pain, restlessness and hypotension. He was noted to pass dark urine and his bilirubin subsequently rose to 51µmol/l. The unit was confirmed to be ABO identical and the antibody screen was negative pre- and post-transfusion. Further retesting of the pre-transfusion sample including a repeat crossmatch confirmed the negative findings, but samples were not referred to a reference laboratory. He has not received further red cells in this hospital and there is no further follow-up.

Anaphylactic/anaphylactoid reactions

Five anaphylactic/anaphylactoid reactions were reported. There was one case of major morbidity (case 6) and a second patient already on the intensive therapy unit (ITU), required further inotropic support following initial resuscitation.

Case 6

A 37 year old female was known to have severe atopic eczema, asthma and to be allergic to peanuts. As a toddler, she developed urticaria following ingestion of peanut butter but by the age of 16 years had obstructive laryngeal oedema on inhaling peanut powder. She was not allergic to latex and had no previous transfusion history.

Following a caesarean section for haemolysis, elevated liver enzymes, and a low platelet count (HELPP) syndrome and a post-partum haemorrhage, she was transfused with 2 units of red cells when she returned to the ward. The first unit was transfused uneventfully. The second unit was commenced after an interval of 2 hours and within the first 5 minutes she had difficulty breathing, collapsed and had a cardiac arrest from which she was successfully resuscitated.

Serial mast cell tryptases showed an elevation to 60.1ug/l 2 hours after the arrest with a fall to normal levels 24 hours later, in keeping with mast cell degranulation. Subsequent investigation of the patient revealed a normal IgA level, a total serum IgE level >5000u (NR 5-120) and strongly positive IgE radioallergosorbent test (RAST) to nuts, eggs and wheat.

Given the temporal relationship of her reaction to the second unit of red cells, the question was raised as to whether this donor had eaten any of the allergens to which she was known to be allergic. However both donors' sera were tested for peanut protein with negative findings. An alternative explanation of the patient having inadvertently ingested a known allergen was thought less likely given her immediate post-operative state.

Of the 4 remaining cases, 3 were not investigated and the fourth was not IgA deficient.

Allergic Reactions

There were 8 allergic reactions reported with features as noted below:

Table 19

Clinical features of allergic reactions to red cells

Case No.	Fever	Rigors	Hypertension	Rash	Dyspnoea	Hypoxia	Angioedema
15	x	x	x		x	x	
16	x				x		x
17	x			x			
7	x	x	x		x		
18				x	x	nk	x
19	x				x	x	
20		x			x	nk	
21	x		x		x	x	

(nk = not known)

In 4 of the cases, fever and dyspnoea (without recorded wheeziness) were the only manifestations, with reduced oxygen saturation, when measured. HLA antibodies were recorded in 2 but not tested for in the remaining 2.

In 5 out of the 8 cases IgA levels were measured, with one IgA deficiency but no anti-IgA.

Case 7

A 22 year old male climber had a combined tibia/fibula fracture and required a post-operative transfusion. After 50mL, he became febrile with rigors, wheezy, hypertensive and vomited. His white cell count was normal at 7.2 x 10^9/l before the transfusion, but fell to 1.6 x 10^9/l immediately following with only 0.02 x 10^9/l neutrophils. He responded promptly to hydrocortisone, antihistamine and a bronchodilator. The neutrophil count returned to normal within 5 hours. Cultures of the patient and the red cells were negative, a mast cell tryptase was not performed.

The patient's serum did not contain granulocyte specific antibodies and the transient nature of the neutropenia suggests that margination could have occurred. The chest x-ray (CXR) showed no abnormality.

Febrile reactions

Of the 17 febrile reactions reported this year, 3 are included in the report. Two were the result of red cell alloantibodies not detectable in the patients' pre-transfusion antibody screen, and the electronic issue and transfusion of incompatible units. An anti-Wr^a caused fever and chills following the transfusion of 140mL red cells, and an anti-Bg^a caused fever towards the end of the transfusion. In neither case were features of haemolysis mentioned.

A third febrile reaction in a 74 year old male resulted in an overnight admission for observations since the reaction provoked chest pain and restlessness.

Of these 17 febrile reactions, sufficiently severe to stop the transfusion, there are only 9 reports of the units being cultured.

Unclassifiable reactions

Case 8

An 83 year old male with a lymphoplasmacytoid lymphoma and an IgM paraprotein had already received 4 units of red cells within the last 48 hours. During transfusion of the fifth unit he became febrile, hypertensive and dyspnoeic. The transfusion was stopped for immediate investigation of red cell incompatibility and then recommenced. The symptoms returned, worse than previously and, since his dyspnoea and wheeziness did not immediately respond to piriton, hydrocortisone and salbutamol,(oxygen saturation 82% on 100% O_2) he required intubation. He recovered within 3 hours. Investigations for TRALI were negative and although the features could be in keeping with a severe allergic reaction, a component of hyperviscosity/fluid overload cannot be excluded.

Case 9

A 32 year old male with sickle cell disease was admitted with an evolving acute chest syndrome and over the following 48 hours he was transfused with 3 units of red cells followed by an exchange transfusion of 6 units. His chest symptoms improved. On the third day he was given a further 2 units of red cells without incident. The transfusion finished at 2340 hours and his observations remained stable until 0600 hours when he had a grand mal fit. He was subsequently noted to be hypoxic and tachypnoeic and required intubation. He then had a cardiac arrest from which he was successfully resuscitated. The CXR showed bilateral pulmonary infiltrates consistent with acute lung injury (ALI).

TRALI was suspected by the intensivists but the last 2 units and the patient's serum tested negative for HLA and granulocyte antibodies. Volume overload was considered in view of his known renal impairment. However in addition to the red cells, other factors including his recent chest syndrome and likely hypoxia during a grand mal fit, could have contributed to the development of ALI.

Reactions in which FFP was implicated

There were 24 reports in this group (one in conjunction with red cells), with one death likely to be due to the transfusion and 2 instances of major morbidity also likely to be due to the transfusion. Eighteen occurred during the transfusion and 6 within 2 hours of the transfusion.

The following reactions were seen:

Table 20

Reactions in which FFP was implicated

Reaction type	Number
Anaphylactic/anaphylactoid	14
Allergic	9
Hypotension	1

Anaphylactic/anaphylactoid

Of the 14 patients in this group, one received solvent detergent treated FFP during plasma exchange and the remainder, standard FFP.

It is questionable whether the FFP was indicated for the cases resulting in mortality and morbidity.

Case 10

A 17 year old male with Burkitt's lymphoma had obstructive jaundice and a coagulopathy, secondary to lymphadenopathy in the porta hepatis. He required intrathecal chemotherapy and FFP was given prior to lumbar puncture, to correct his abnormal coagulation screen.

After receiving 100mL FFP he started to wheeze, and rapidly became hypotensive and had a cardiac arrest. He received adrenaline, antihistamines and bronchodilators prior to the arrival of the cardiac team. Resuscitation was unsuccessful.

The patient had not been given vitamin K which should have corrected the prolonged coagulation screen.

Case 11

A 64 year old male was recovering from an abdominal aortic aneurysm repair. There was minimal fresh blood loss from the wound or drains and a coagulation screen showed a prolonged activated partial thromboplastin time (APTT) of 50 seconds, which the reporters felt to be spurious and possibly due to heparin in the line. However, he was prescribed FFP and within 40 minutes developed an irritant skin rash. Five minutes later he was wheezing and within the following 5 minutes his systolic blood pressure had fallen to 50mm Hg and he had a cardiac arrest. He was ventilated for 24 hours.

Case 12

An 83 year old female on Warfarin had not discontinued this drug prior to an elective femoro-popliteal bypass graft. Consequently she was prescribed FFP pre-operatively. She developed pruritus, angioedema and became hypotensive shortly after commencing the second unit. As a consequence, she sustained a myocardial infarct and was admitted to the coronary care unit (CCU).

Ten of the 14 cases were investigated. None were found to have IgA deficiency. Six investigations included mast cell tryptase, of which one was positive.

Three of the 14 had chest X-rays performed, 2 of which showed bilateral pulmonary oedema.

Allergic reactions (not anaphylaxis)

There were 9 patients in this group.

Four out of the 9 had more than one feature of an allergic reaction (rash, dyspnoea and angioedema).

Four had further investigations but none were IgA deficient. In two, investigations included mast cell tryptase, which were raised in one.

Hypotension

One patient undergoing plasma exchange for thrombotic thrombocytopenic purpura (TTP) experienced hypotension, nausea and hypothermia to 33^{0}C, attributed to the administration of a rapid large volume of cold FFP.

Inappropriate use of FFP

Coagulation results are not available for all cases satisfying the definition of massive transfusion, but these have been included as clinically indicated.

Category	No. of patients	Indication given
Clinically indicated	14	TTP - 2 DIC with haemorrhage - 1 Massive transfusion - 4 Liver disease with intervention - 2 Pre-operative correction coagulopathy - 1 Post-operative bleed with raised INR - 4
Possibly indicated	2	In obstructive jaundice, without trial of Vitamin K prior to lumbar puncture - 1 Postoperative aneurysm repair, prolonged APTT, ? spurious - 1
Not indicated	8	Liver disease with no bleeding - 1 Postoperative, no bleeding - 3 Carcinoma colon, no bleeding - 1 Warfarin reversal prior to elective surgery or for minor haemorrhage - 3

Reactions in which platelets were implicated

There were 20 reactions to platelets, of which 17 occurred during the transfusion, 2 within 2 hours and one within 7 hours following the transfusion. One patient suffered major morbidity, likely to be as a result of the transfusion.

Table 21

Reactions in which platelets were implicated

Reaction type	Number of cases
Anaphylactic/anaphylactoid	5
Allergic	11
Hypotension	3
Unclassifiable	1

Anaphylactic/anaphylactoid reactions

Five patients suffered anaphylactic/anaphylactoid reactions, 3 following the transfusion of pooled buffy coat derived platelets and 2 following apheresis platelets.

One patient initially developed a skin rash and mild dyspnoea. The transfusion was temporarily stopped whilst an antihistamine and hydrocortisone were given. On restarting the transfusion the patient rapidly developed an anaphylactoid reaction.

Three of the 5 who were receiving platelets in a day ward setting required admission.

All were multi-transfused recipients. Three were investigated for HLA and human platelet antigen (HPA) antibodies with negative findings. Three of the 5 are still platelet dependent and receiving platelets in platelet suspension medium (PSM) with no adverse reactions.

Allergic reactions

Eleven patients suffered allergic reactions.

Seven out of the 11 had more than one feature of an allergic reaction (rash, dyspnoea and angioedema).

Five were investigated, 2 for IgA deficiency and 2 for HLA antibodies, with negative findings. Two of the 5 were also tested for mast cell tryptase, one of which was increased.

Hypotensive reactions

Three patients, who were not receiving angiotensin-converting enzyme (ACE) inhibitors, had hypotension alone.

Unclassifiable

Case 13

A 24 year old female with high grade Non Hodgkins Lymphoma (NHL), was platelet and red cell dependent post allograft. Within 5 minutes of the transfusion of apheresis platelets, she started to sweat profusely, complained of 'tightness' in her chest, developed a tachycardia and her BP rose to 170/110. On examination she had reduced air entry with crackles and an oxygen saturation of 75% and subsequently had a respiratory arrest.
The patient was an out-patient who had received no other parenteral fluids that day, making volume overload very unlikely. Cultures of the patient and the platelet concentrate were negative.
A CXR performed following the arrest showed 'ground glass' changes, rather than bilateral pulmonary oedema. She recovered on ITU but was subsequently found to have a large intracerebral bleed, which may have been precipitated by the reaction.

Reaction in which granulocytes were implicated

There was one case of an anaphylactic/anaphylactoid reaction with major morbidity.

Case 14

A 32 year old male with aplastic anaemia received granulocytes from a family member. During the transfusion, his blood pressure dropped to unrecordable levels and he lost consciousness. He was successfully resuscitated with hydrocortisone, piriton and adrenaline and subsequently required amiodarone for adrenaline induced ventricular tachycardia.
He was admitted to HDU.

Response times

The majority of patients were seen as soon as possible by a doctor, and a Consultant Haematologist was also consulted for reactions involving red cells or platelets.

Table 22

Time taken for patient to be reviewed by a doctor

Response times	Red Cells (23)	FFP (24) *	Platelets (21)≠
< 15 minutes	12	20	15
< 30 minutes	3	1	3
< 60 minutes	2		1
> 60 minutes	2		
Unknown	4	3	2
Total	23	24	21
Involvement of Haematologist	**19**	**10**	**15**

* includes case in which both FFP and red cells were transfused
≠includes case involving granulocyte concentrate

Changes made to procedures

Two hospitals have reinforced the need to avoid elective transfusions during night shifts as a result of reactions being inadequately managed at this time.

Reporting of acute transfusion reactions

All but 1 acute transfusion reactions were reported to the hospital laboratory and the majority were also reviewed at the Hospital Transfusion Committee. Three of the 5 haemolytic reactions involved the Transfusion Centre and other reactions were reported to them when samples were referred for investigation.

Table 23

Reporting of reactions to the Hospital Transfusion Committee, Hospital Laboratory and the local Transfusion Centre

Reported to	Red Cells (23)	FFP (24) *	Platelets (21) ≠
Hospital Transfusion Committee	20	16	16
Hospital laboratory	23	24	20
Transfusion centre	18	7	12

* includes case in which both FFP and red cells were transfused
≠includes case involving granulocyte concentrate

COMMENTARY

- Case 1 illustrates the difficulties posed by patients with complex antibodies requiring repeat transfusions.
- There is still significant inappropriate prescription of FFP.
- There has been an increase in the number of allergic or anaphylactic/anaphylactoid reactions reported due to red cells.
- In only 9/17 patients reported to have significant febrile reactions to red cells were bacterial cultures performed.
- The reactions cause by red cell alloantibodies (anti-Wr^a and anti-Bg^a), not detectable using screening cells meeting BCSH recommendations, did not result in haemolysis.
- Transfusion reactions occurring at night or in a community setting may not be managed as promptly.

RECOMMENDATIONS

- Pre-transfusion testing on patients who have been recently transfused and require further transfusion should be carried out in accordance with BCSH Guidelines[21] relating to the timing of pre-transfusion samples.

  Action: Hospital transfusion laboratories.

- BCSH Guidelines[22] on the management of anticoagulation in the peri-operative period and on the management of excessive anticoagulation should be followed. Excessive anticoagulation with minor haemorrhage should be treated by stopping the drug and if necessary with intravenous vitamin K.
- BCSH guidelines[9] for the use of FFP should be followed. Its use for the correction of abnormal coagulation results in the absence of bleeding is not justified.

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

- All serious transfusion reactions must be fully investigated. Bacterial cultures must be taken in a febrile reaction, when the rise in temperature exceeds 1.5^{0}C or the reaction is otherwise sufficiently severe to merit discontinuing transfusion. An update of BCSH guidelines is in progress.

  Action: Consultant haematologists with responsibility for transfusion should implement current best practice.[12,13]

- Blood should not be transfused outside of core hours unless clinically essential.

  Action: Hospital CEOs, consultant haematologists with responsibility for transfusion together with HTCs and HTTs.

- Against the background of a trend towards provision of care closer to the patient, there is a need for a standard of practice to be developed for transfusion in the community setting, including provision for appropriate management and reporting of adverse reactions and events.

  Action: UK National Blood Transfusion Committees to facilitate and co-ordinate.

8 Delayed Transfusion Reactions

Definition

Delayed transfusion reactions are defined 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.

Twenty-nine delayed transfusion reaction (DTR) questionnaires were received, one of which was transferred to the Acute Transfusion Reaction chapter.

This chapter describes the main findings from 28 completed questionnaires.

Patients

11 males and 17 females

Ages ranged from 8 to 89

Definition of severity of reaction/ clinical sequelae

Symptoms and signs are 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

Severity

One patient required ICU admission and subsequently died, but this was thought to be unrelated to the transfusion (Imputability 0).

6 patients were asymptomatic with a positive DAT and antibody development only (Group 1).

22 patients had evidence of increased red cell destruction but without renal impairment:

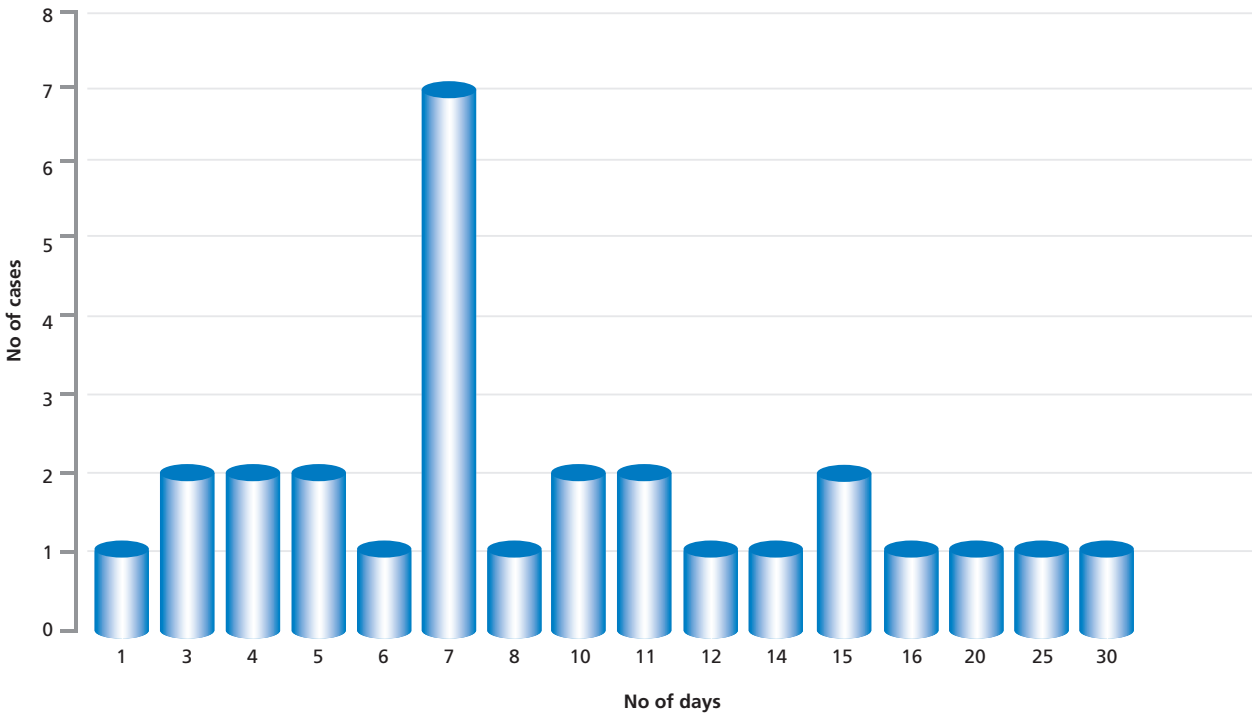
- In 7 cases the only sign was a fall in haemoglobin, with or without a positive DAT and spherocytes (Group 2)
- In 15 cases there was a fall in haemoglobin and a raised plasma bilirubin, although clinically detectable jaundice was only reported in 5 cases (Group 3). One of these patients died (case 9 - see vignette), with no evidence that the death was related to the transfusion and no detectable alloantibody.

Sequelae

6 patients were already on ICU, 5 required admission to the ward from outpatients or day care, and at least 5 required further transfusion. Only one was reported as posing a 'risk to life' (case 17).

Figure 8

Time relationship to transfusion



Median = 7 days

Range = 1 to 30 days

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; in asymptomatic cases this relates to the number of days that elapsed before a repeat sample happened to be tested.

There were 3 cases where symptoms were noted within 72 hours of transfusion: in the first (case 2) no earlier recent transfusion was reported and repeat testing of the pre-transfusion sample was not undertaken; in the second (case 12 - see vignette) another transfusion had been given 12 days earlier; in the third (case 27), another 3 transfusions had been given in the preceding 16 days, the most recent of which was 5 days before the DHTR. In both of these latter cases the earlier transfusions were more likely to have been implicated in the DHTR than the reported transfusion.

Serological findings

Kidd antibodies were the most commonly implicated, in 11/28 (39%) of cases, either singly or in conjunction with other specificities. Two patients had no detectable antibodies and are described as vignettes. Table 24 shows the specificity of new antibodies in plasma and eluate, and the number of days post transfusion. Tables 25 and 26 show new specificities by blood group system and severity, respectively.

Table 24

Case number	New antibody (ies) in plasma	Antibodies in Eluate	Comments	No. days post tx
1	Anti-Jk^{b}	No eluate performed		7
2	Anti-Jk^{a}	No eluate performed	Pre-existing anti-E+K. No record of recent transfusion	3
3	Anti-Jk^{a}	No eluate performed	Already in ICU	10
4	Anti-K + E	Anti-E		30
5	None in plasma	Non-specific reactions	Further transfusion required	25
6	Anti-Fy^{a}	No eluate performed		7
7	Anti-Jk^{a} + c	No eluate performed	Required admission	15
8	Anti-S	No eluate performed	Required admission	14
9	None	No eluate performed	Sharp rise in bilirubin. DAT negative. Died unrelated to transfusion	4
10	None in plasma	Anti-Jk^{a}		5
11	Anti-E + Jk^{a}	Anti-E + Jk^{a}		5
12	Anti-S	Anti-S	Also transfusion 12 days previously	1-2
13	Anti-M	No eluate performed	Required admission. History of anti-C+Fy^{a}+S+K+Kp^{a}+Kn^{a}+McC^{a}. DAT negative.	7
14	Anti-Lu^{a} + Jk^{b}	Eluate negative	Required admission	11
15	Anti-S	Anti-S		20
16	Anti-Fy^{a} + E (E enzyme only)	No eluate performed	Already in ICU. Antibody screen weakly positive on retrospective testing.	7
17	M+cold agglutinins	No eluate performed	Already in ICU. Pre-existing anti-K+E. Anti-M previously identified elsewhere.	6
18	Anti-c + E	Anti-E	Required admission and further transfusion	16
19	Anti-C	Eluate negative		10
20	Anti-Fy^{a} + E (E enzyme only)	Anti-Fy^{a}	Already in ICU	11

21	None	Elulate negative	DAT positive but anti-JK[a] subsequently identified at day 11 - 4 days post DHTR	7
22	Anti-Jk[b]	No eluate performed	Pre-existing anti-C+D	4
23	Anti-Fy[a]	Anti-Fy[a]		8
24	No new abs	Anti-Fy[a]	Pre-existing anti-c+E+Fy[a]+Kp[a] Fy(a-) units transfused	7
25	Anti-c + E + Jk[a]	No eluate performed	Further transfusion required	15
26	Anti-Jk[a] + E + Ab to low incidence Ag	No eluate performed	Further transfusion required	12
27	Anti-Fy[a]	Anti-Fy[a]	Already in ICU. Also transfused on 3 occasions during the previous 16 days	3
28	Anti-Fy[a]	No eluate performed	Already in ICU	7

Table 25

New specificities by blood group system

Antibody specificity by blood group system	Number of cases	Sole *new* antibody
Kidd		
Jk[a]	8	4[1]
Jk[b]	3	1
Rh		
C	1	1
E	7	0
c	3	0
Kell		
K	1	0
Duffy		
Fy[a]	6	4
MNSs		
S	3	3
M	2	2[2]
Other		
Lu[a]	1	0
Unspecified low incidence	1	0
Non-specific	1	1[3]

1 - one detected only 4 days post DHTR and one detected in eluate only
2 - one also developed cold agglutinins
3 - in eluate only

Table 26

Antibody specificity by severity definition, where antibodies in brackets relate to pre-existing specificities

Group 1		Group 2		Group 3					
Case No.	**Ab specificity**	**Case No.**	**Ab specificity**	**Case No.**	**Ab specificity**	**Case No.**	**Ab specificity**	**Case No.**	**Ab specificity**
15	S	1	Jk^a	2	Jk^a (E+K)	10	Jk^a (eluate only)	22	Jk^b (C+D)
18	c+E	4	K+E	3	Jk^a	12	S	24	None (multiple) Fy^a in eluate
19	C	7	c+Jk^a	5	Non spec	13	M (multiple)	26	Jk^a+E
23	Fy^a	11	E+Jk^a	6	Fy^a	14	Lu^a+Jk^b		
27	Fy^a	16	Fy^a+enz E	8	S	17	M + cold aggs (K+E)		
28	Fy^a	25	c+E+Jk^a	9	None	21	Jk^a (4 days post DHTR		

Use of plasma/serum

In 27 cases plasma was used (96%) for pre-transfusion (one not stated); 23 also used plasma for post transfusion testing (5 not stated).

Serological Techniques Used

These broadly reflected those used in clinical practice.

One BioVue user used an inappropriate cell:plasma ratio and one low-ionic-strength-solution (LISS) tube suspension user used too high a cell concentration and an inappropriate plasma:cell ratio. However, in neither of these cases is there any evidence that the causative antibody was missed in the pre-transfusion sample.

Use of eluates

Only 14 (50%) stated that an eluate made from the patient's post transfusion red cells was tested for antibody, though a further 4 did not answer the question. 10 were performed by reference labs and 4 in-house. In 10 cases a specific antibody(ies) was identified, and in one case this was the only way of identifying the anti-Jk^a, since the antibody was not detected in the plasma. In 3 cases the eluate was negative, and in one non-specific reactions were observed; in this latter case, no free antibody was detectable in the plasma. In 4 cases the eluate demonstrated a single specificity where a mixture of new antibodies was present in the plasma, including one case of anti-c+E, where only anti-E was demonstrable in the eluate.

Retrospective testing findings

Retrospective testing of the pre-transfusion sample was undertaken in 13 (46%) cases; the same result as in the original (pre-transfusion) testing was obtained in 11 of these. In one of the other 2 cases (case 16), the antibody screen was found to be weakly positive on retrospective testing using the same DiaMed IAT technique, although the reporter did not state whether the anti-Fy^a was actually identified; this followed an earlier transfusion within the previous two weeks. In the second case (case 13 - see vignette) some weak reactivity against 2 panel cells was noted in a sample from a patient with multiple other antibodies, but no specificity could be assigned; identification in this patient was complicated by Knops/McCoy activity.

Clinical management and review

15 (54%) of cases were referred to the Blood Centre Reference Laboratory and 25 (89%) to the HTC. Twelve of these were reported to both.

Vignettes

No antibodies detected - no clear evidence of a DHTR (imputability 1)

Case 5

A 34 year old female patient with post-operative bleeding required 3 units of red cells. 26 days later her DAT was strongly positive (IgG) and spherocytes were noted on her blood film. Samples were referred to the blood service red cell reference laboratory, but no antibodies were detected in the plasma, and an eluate made from the patient's red cells showed no specificity. The Hb dropped by 3g/dL between day 25 and day 27, with a small rise in bilirubin, but no signs of bleeding. She required a further transfusion, which was followed by a similar drop in Hb over the next 48 hours. During this time she also became pyrexial, and Candida was detected in the blood cultures. The patient was subsequently transfused with R_1R_1 K- red cells, although the presence of transfused red cells made her phenotype impossible to determine; her Hb then remained stable.

Case 9

An 84 year old female patient received 12 units of red cells over an 8 day period for rectal bleeding. 3 days after the most recent transfusion, she became jaundiced and was suffering from acute respiratory distress syndrome (ARDS); her bilirubin rose from 20 to 127 µmol/L and reached a peak of 231 2 days later. The Hb also fell, but it is unclear whether this was due to bleeding or the transfusion or both. She received a further 2 units 9 days later and once again her bilirubin rose from 167 to 291µmol/L. A DAT was not performed until 8 days later when it was negative. The patient was subsequently admitted to ICU and died, but this was thought to be unrelated to the transfusion.

Difficult to classify

Case 10

A 75 year old female patient received 3 units of red cells for an inferior mesenteric artery bleed. A group and save sample tested 3 days previously gave a positive antibody screen and a positive DAT (both IgG and complement coating). The sample was referred to the blood service red cell reference laboratory 2 days later, where anti-Jk^a was eluted from the patient's red cells, although no plasma antibody was detected. It is not clear why non-phenotyped blood was issued based on an empirical crossmatch. The patient did not get the expected increment in Hb and had a raised bilirubin 5 days after transfusion; however, the reporter indicated that these signs were indistinguishable from those due to multiple disease factors.

This case is difficult to classify: the anti-Jk^a presumably developed as a result of a transfusion given 14 to 28 days previously and was clearly present in the pre-transfusion sample. Whether the blood was transfused without Jk^a typing, due to a lack of communication or a misunderstanding is not clear. It is also unclear which symptoms were due to a transfusion reaction and which were due to disease. This could therefore equally be classified as an acute transfusion reaction or an IBCT.

Case 12

A 7 year old female patient with sickle cell disease was admitted with a painful crisis and a Hb of 6.6g/dL. The antibody screen was negative and she was transfused with a unit of red cells. 12 days later she was re-admitted, again with painful crisis. Her Hb was initially 8.5g/dL but on repeat was found to be only 4.5g/dL. The antibody screen was negative, and although the DAT was weakly positive (due to both IgG and complement coating), this was not investigated until 3 days later because it was a Friday night. She again received one unit of red cells. Over the following 2 days, dark urine was noted and laboratory tests indicated that she had no increment in Hb and a raised bilirubin; a DHTR was suspected. Anti-S was identified post transfusion and was eluted from the patient's red cells. Both red cell units were found to be S positive. The patient recovered quickly.

This case was reported as a DHTR occurring 1-2 days post the second transfusion. However, the timing and the pre-transfusion DAT, suggest that this is more likely to be a combination of a DHTR due to the transfusion given 12 days previously and an acute haemolytic transfusion reaction (AHTR) following the 2nd transfusion of S positive blood. The picture is also complicated by the sickle cell crisis.

More unusual/interesting cases

Case 13

A 69 year old woman with a myeloproliferative disorder and a history of multiple red cell transfusions, was known to have anti-K+Kp^a+S+C+Fy^a+Kn^a/McC^a, although only the anti-K and -Kp^a had been recently detectable. On this occasion the pre-transfusion sample showed further reactions and the sample was sent to the reference laboratory for further investigation and crossmatching. The reference laboratory found anti-Kn^a and McC^a, but no convincing evidence of new antibodies and provided 3 units of crossmatched blood, 2 of which were transfused 4 days later. Seven days post transfusion the patient developed left upper quadrant pain, progressive splenomegaly and jaundice, and her Hb dropped. The reference laboratory was sent a post-transfusion sample on which it made an immediate verbal report of anti-M; both transfused units were subsequently confirmed as M positive. Five days later another transfusion was required and M negative blood was supplied. After 200mL of the first unit, the patient developed fever and rigors, and passed dark urine, requiring admission from the day ward. Spherocytes and hyperbilirubinaemia were later noted. The DAT was negative following both transfusions and no eluates were performed. Bacterial contamination of the unit was excluded and the cause of the acute reaction was not established. The acute reaction has also been reported in the ATR chapter (case 1).

This is an unusual case; the anti-M was reported to have been weak (2+) and the DAT was negative, so would be an unusual cause of a DHTR; however there appears to be no obvious alternative cause. Anti-M has been excluded as a cause of the AHTR since the latter units transfused were M negative.

Case 2

A 72 year old female patient was bleeding following over-anticoagulation with Warfarin, and required a 3 unit red cell transfusion The pretransfusion antibody screen was positive and anti-E+K was identified in the plasma using a BioVue IAT and 2-stage enzyme technique; crossmatch compatible, antigen negative blood was transfused. 3 days later the patient passed dark urine and became jaundiced. Laboratory investigations demonstrated a raised bilirubin, a falling Hb and spherocytes. Anti-Jk^a in addition to anti-E and -K was identified in the plasma, and the DAT was positive, due to both IgG and complement coating. No eluate was performed and the pre-transfusion sample was no longer available for testing.

Although 3 days is a shorter interval than is classically expected for a DHTR, this patient had no recent history of transfusion and there was no indication of anti-Jk^a in the pre-transfusion sample, even using a 2-stage enzyme technique.

Case 17

A 16 year old male patient required a transfusion in ICU following emergency surgery. Anti-E+K were identified in his plasma and one unit of antigen negative, crossmatch compatible blood was transfused. 6 days later he passed dark urine and became jaundiced. Laboratory investigations demonstrated a raised bilirubin and a falling Hb; the DAT was positive due to both IgG and complement coating and anti-M plus a non-specific cold autoagglutinin were detected in the plasma and confirmed by a reference laboratory. An eluate was not performed. Retrospective testing of the pre-transfusion plasma using the same DiaMed IAT technique confirmed that only anti-E and anti-K were detectable pre-transfusion. Anti-M had apparently been identified by a different hospital 2 months previously, but this information was not available until after the patient had been transfused.

Case 24

An 84 year old male patient with myelodysplasia and a history of transfusion (> 3 months previously) required several units of red cells over a 2 day period, following a total hip replacement. The patient was known to have anti-c+E+Fy^a+Kp^a, and crossmatch compatible antigen negative blood was transfused. 7 days later it was noted that the patient had increased reticulocytes and a raised bilirubin. The reference laboratory confirmed that the DAT was positive due to IgG coating, but that no new antibodies were detectable. Anti-Fy^a was identified in an eluate made from the patient's red cells, despite all the transfused units apparently being confirmed as Fy(a-).

COMMENTARY

- According to the literature, DHTRs caused by anti-M are rare. Anti-M was found in two cases of DHTR this year, with clinical signs of red cell destruction in both cases; i.e. dark urine, falling Hb and raised bilirubin 6 to 7 days post transfusion. Both of these cases had complex serology, with pre-existing alloantibodies, and in one case newly developed cold agglutinins. Unfortunately in neither case was extensive investigation undertaken to prove whether or not anti-M was responsible for the red cell destruction. It is particularly difficult to draw any conclusions in case 17, since there were no details available regarding the patient's underlying diagnosis, the DAT was positive for complement as well as IgG and anti-M does not bind complement, and the transfused unit was not typed for M. There have been 5 cases in previous SHOT reports where anti-M has been identified as a new specificity; in 4 of these, additional specificities were also identified, but there is no record of eluates being performed.
- In all cases (where an answer was given) plasma rather than serum was used for both pre and post transfusion investigations. It is known that weak complement binding antibodies, e.g. some examples of anti-Kidd, may be missed when using plasma, unless more sensitive techniques are used, e.g. enzyme IAT.
- In 3 cases DHTRs were reported to have occurred within 72 hours of the implicated transfusion. However, in 2 of these, earlier transfusions were more likely to have been implicated in the reaction.
- Only 50% of investigations included testing an eluate made from the patient's red cells. Where a mixture of antibodies is present, an eluate may help to distinguish which specificity(ies) is more likely to be implicated in a haemolytic reaction. Furthermore, the implicated antibody may only be present in an eluate, as in case 10. Identification of all specificities present is essential if further haemolytic reactions are to be prevented.
- As in previous years, communication problems have contributed to DHTRs, where information about previously known antibodies has not been available at the time of a subsequent transfusion.

RECOMMENDATIONS

- All cases of suspected AHTR and DHTR should be appropriately investigated, and ideally referred to a reference laboratory. Referring hospitals should make it clear to reference laboratories that they are investigating a DHTR to ensure that timely, appropriate tests are undertaken. Clinical details should be completed on the request forms and the donation numbers of the units transfused should be included, so that their phenotype can be determined. Reference laboratories should ensure that investigation of DHTRs includes testing an eluate made from the patient's red cells when the DAT is positive.

  Action: Hospital blood transfusion laboratories and reference laboratories

- Inconclusive antibody screens should be investigated prior to transfusion and results confirmed with a reference laboratory if necessary.

  Action: Hospital blood transfusion laboratories

- Investigation of a suspected DHTR should include retesting of the pre-transfusion sample (where still available) by different or more sensitive techniques. Consideration should also be given to requesting clotted samples for investigation of suspected DHTRs and using polyspecific antihuman globulin (AHG). These actions may involve referral to a reference centre.

  Action: Hospital blood transfusion laboratories.

- Hospitals and reference laboratories should be encouraged to publish case reports of DHTRs, after appropriate investigations have been undertaken, and where the implicated antibody is not recognised as a common cause of such reactions.

  Action: Hospital blood transfusion laboratories and reference laboratories.

- In line with recommendations made in the BCSH Guidelines,[21] consideration should be given to issuing antibody cards or similar information 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: The CMO's NBTC and its counterparts in Scotland, Wales, and Northern Ireland.

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

  Action: BBTS and BCSH.

9 Transfusion Related Acute Lung Injury

Definition

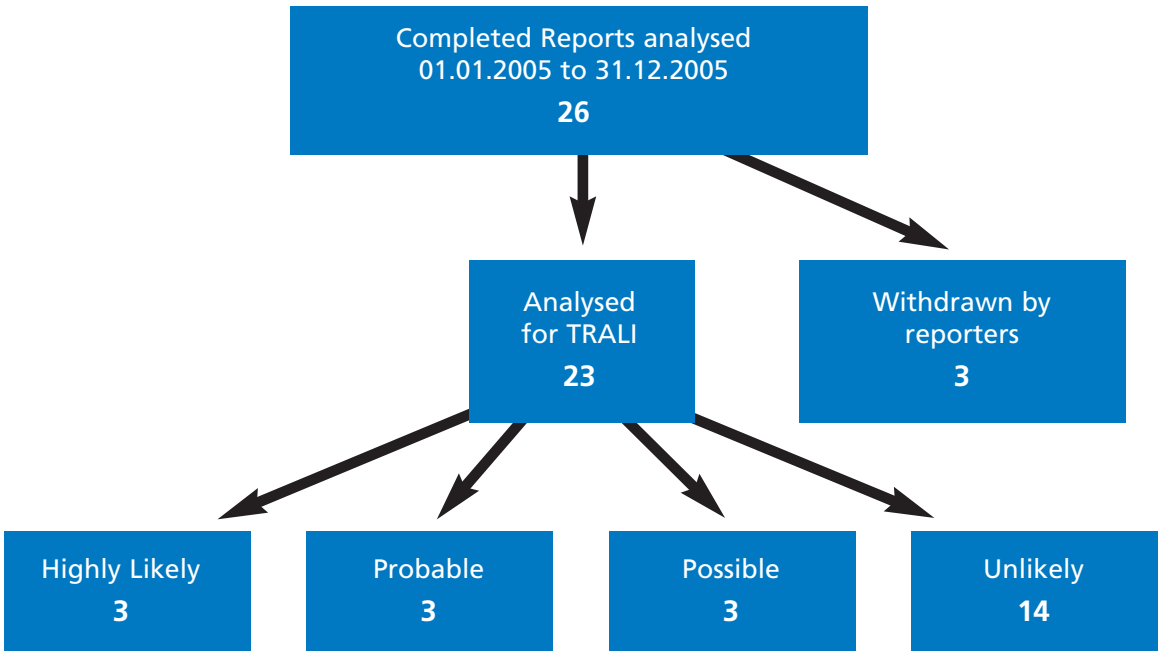
Transfusion-related acute lung injury was defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates occurring during or in the 24 hours after transfusion, with no other apparent cause.

Twenty-six case reports of suspected TRALI were received in this reporting year. Of these, 3 were subsequently withdrawn by the reporters for a variety of reasons.

Twenty-three cases were analysed. Of these, 6 patients died, 16 suffered short-term major morbidity and one had long term morbidity. Of the 6 patients who died, death was possibly due to TRALI in 2 cases (imputability 1) and unlikely to be related in 4 cases (imputability 0). **Figure 9.**

Figure 9

Summary of cases reported



The 23 reports received in 2005 related to transfusions which occurred between December 2003 and October 2005 inclusive. Two reports related to transfusions in 2003, 10 related to 2004 and 11 to 2005.

Assessment of TRALI reports

TRALI can be a difficult diagnosis because there is no single test for this condition and it is easily confused with other causes of acute lung injury and cardiogenic pulmonary oedema. If the clinical picture occurs in a previously fit patient and relevant leucocyte antibodies are found, the diagnosis is straightforward. Often however, it occurs in patients who have other risk factors for the development of ALI or ARDS. When TRALI is suspected, a detailed assessment of the clinical event is required together with investigation of the patient and donors. Early discussion with the Blood Service is recommended and blood samples (ethylenediaminetetraacetic acid (EDTA) and clotted) from the patient should be sent promptly to a Blood Service Reference laboratory. Clinical factors which were taken into consideration in the assessment of reported cases included: pre-existing cardiac, pulmonary or other disease e.g. leukaemia with pulmonary leucostasis; time between transfusion and respiratory deterioration; radiological features; possibility of infection; other risk factors for ALI/ARDS; evidence of circulatory overload and/or impairment of cardiac function and time to respiratory recovery with supportive treatment.

Results of TRALI investigations may not be definitive. Because of the frequency of leucocyte antibodies in the donor population, donor antibodies would also be found in many uneventful transfusions if they were similarly investigated. In an NBS study of 1166 female donors, HLA antibodies were found in 14.5% (personal communication, Dr S. MacLennan).

Two Transfusion Medicine Specialists who also reviewed cases last year have assessed the likelihood of TRALI in each case. All cases reported to the NBS have also been initially assessed by 2 Intensive Care Specialists. Reports were graded on the basis of clinical features and available laboratory results. Complete results of relevant serological investigation were not available in 7 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	Clinical and radiological features of cases reported as TRALI
TRALI Table 3	Treatment, investigation results and likelihood of case being TRALI

Patient characteristics

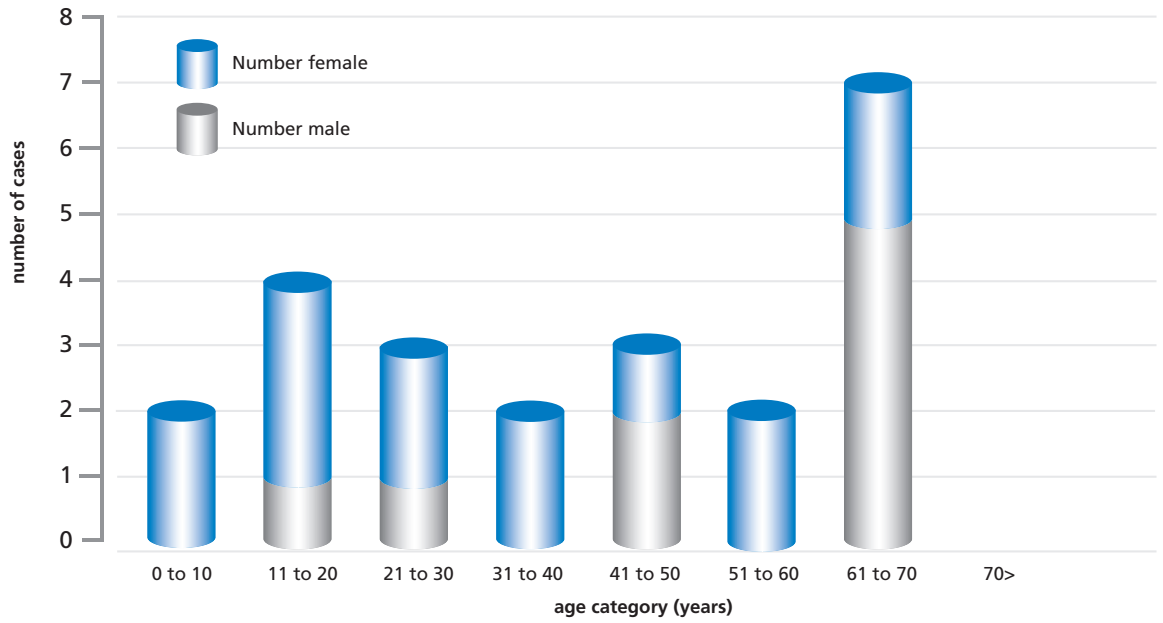
Patient characteristics are tabulated in TRALI Table 1 on the SHOT website www.shot-uk.org

Age and sex

An analysis of cases by age and sex is shown in Figure 10. Cases of suspected TRALI were reported in patients aged from 3 to 70 years. Four patients were under 18 years of age. More patients were female (14) than male (9). Analysis of 186 suspected TRALI cases reported to SHOT from 1996 to the present shows a slight excess in female patients (100 cases, 53.8%) compared with males (84 cases, 45.2%), in 2 cases the sex of the patient is not recorded (1%).

Figure 10

TRALI reports analysed according to age and sex

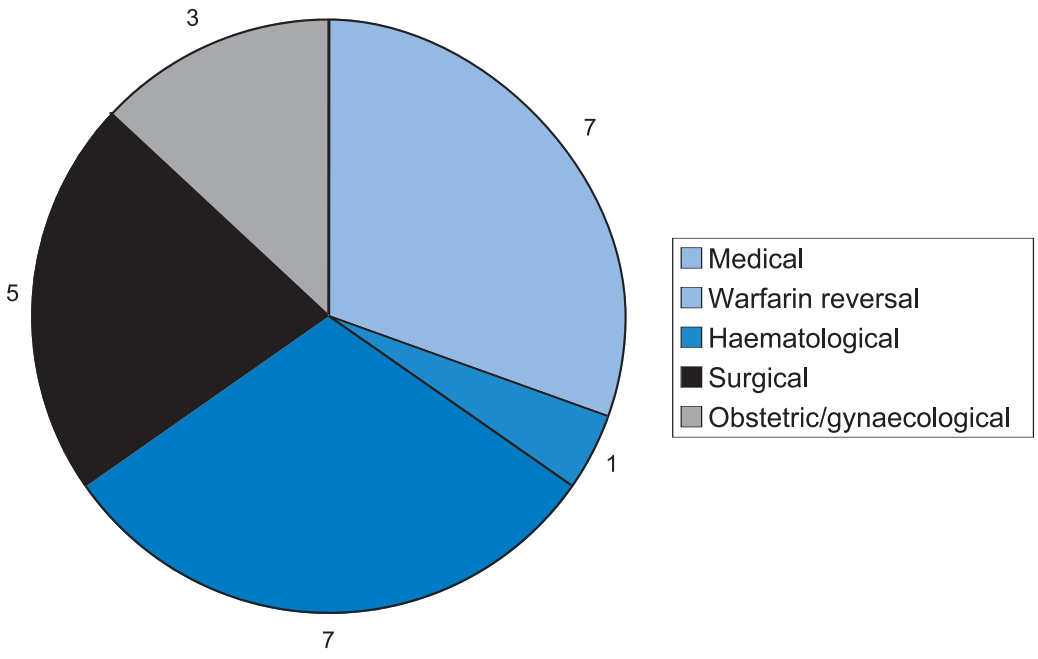


Reason for transfusion

Reports have been analysed according to the reason for transfusion (Figure 11). The most frequent underlying reasons for transfusion were haematological and medical (7 cases, 30% each); surgical procedures accounted for five (22%) cases. Obstetrics and Gynaecology specialities contributed 2 and 1 cases respectively. One report concerned the use of FFP for Warfarin reversal in a patient with a GI bleed; details of coagulation investigations were not provided.

Figure 11

TRALI reports by indication for transfusion



Clinical features

Clinical presentation

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

All suspected cases were reported to have been hypoxic and 19 (83%) patients were treated in Intensive Care Units. Sixteen patients received mechanical ventilation of whom 4 were already on ventilators at the time of the incident. The clinical descriptions of reactions suspected to be TRALI were very similar for the 6 patients in whom the diagnosis was subsequently supported by serological results and for the 17 cases without such immune evidence. Fever was reported in 8 of 19 patients, for whom this was recorded, with similar numbers in the group with serological support (3 of 6, 50%) and in those without (5 of 9, 56%). Hypotension was reported as part of the reaction in 14 of 21 cases. This feature was reported in 3 of 6 patients with supporting serological evidence and 11 of 15 patients without. Signs of heart failure were recorded in 1 of 22 cases and in this case TRALI investigations were negative.

Patient outcomes

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

Six patients died but the majority of patients (16) made a full recovery from the episode. One patient suffered long-term morbidity with residual cerebral and pulmonary damage following probable TRALI. Of those 6 patients who died, 3 were assessed as unlikely to be TRALI, 1 as possible, 1 as probable and 1 as highly likely. Death was considered possibly related to TRALI in 2 cases (imputability 1) and unlikely to be associated with TRALI in 4 cases (imputability 0).

The overall survival of all reported cases was 74%; in the subgroup of 6 cases with proven leucocyte incompatibility survival was 83% and in the 10 patients where incompatibility was excluded survival was 70%. The case with persisting cerebral and pulmonary 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 routinely investigated but none was identified with relevant antibodies. The UK has excluded individuals transfused after January 1st 1980 from donating since April 2004.

Laboratory results

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

All cases were referred to the local Blood Centre for investigation and 20 of 23 cases were subsequently investigated at Reference Laboratories. Complete TRALI investigation results were achieved in 16 cases and partial investigation results for 4 cases. Laboratory investigations were not undertaken in 3 cases; 1 of these had involved massive transfusion with multiple ARDS risk factors and the reason for not investigating the other 2 cases was not clear.

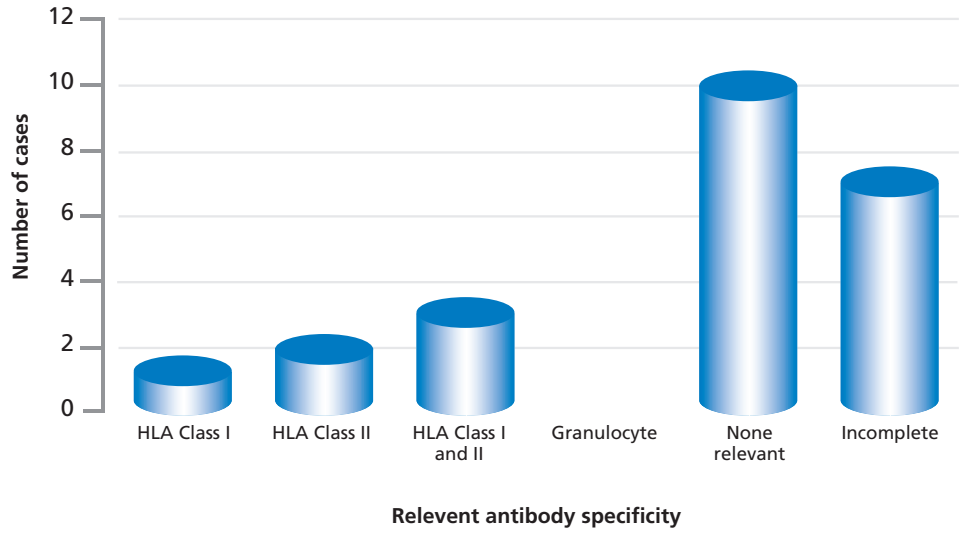
Donor antibodies

Relevant donor leucocyte antibodies (i.e. donor HLA or granulocyte antibody corresponding with patient antigen) were found during investigation of 6 of 16 (37.5%) complete case investigations this year. This compares with relevant antibody identified in 12 of 17 complete investigations in 2004 (70%) and 21 of 30 in 2003 (70%). The reduction in the proportion of cases with relevant antibodies this year is likely to be linked to the reduction in antibody positive FFP cases. It is also possible that more cases are being reported which are not TRALI. This year all 6 cases with relevant donor antibodies involved anti-HLA corresponding with patient HLA. One case involved HLA Class I antibody alone, 2 cases involved HLA Class II alone and in 3 cases both HLA Class I and II antibodies corresponded with patient HLA. No granulocyte antibody was identified with proven specificity for patient antigen. In 1 case an IgM only granulocyte antibody was identified but confirmation of reactivity with patient cells was not possible. In another case, HNA 2a specific antibody was identified but fresh cells were not available from the patient for HNA 2 phenotyping because she had died; HLA antibody with A2 specificity antibody had also been identified in another donor for this HLA A2 positive patient. In a further case, a female donor was found to have HNA 1a specific antibody but the recipient was negative for this antigen. In 10 cases relevant antibodies were excluded and 7 investigations were incomplete.

Analysis of the results of investigation for donor white cell antibodies is shown in **Figure 12.**

Figure 12

Analysis of results of donor antibody investigations



Patient antibodies

Leucocyte antibodies were found in 7 patients, all were HLA antibodies. In 2 of these cases a match was found with donor antigen and in 5 cases it was not established whether the antibody had donor specificity. Investigations for patient HLA or granulocyte antibodies were negative in 11 cases and five patients were not tested. It is considered unlikely that leucocyte antibodies in patients have relevance to TRALI pathogenesis in the context of component leucodepletion.

Components

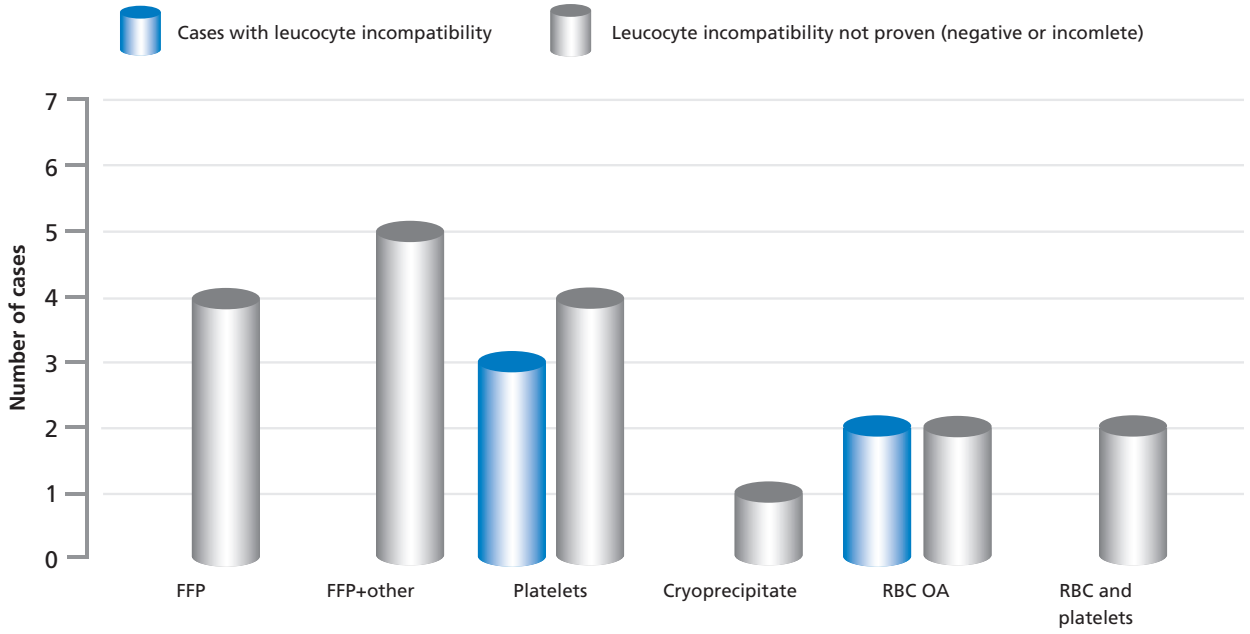
Details of all implicated components are tabulated in TRALI Table 1 on the SHOT website www.shot-uk.org

Platelets were the most commonly implicated component with proven relevant leucocyte antibodies (3 cases; 1 apheresis and 2 buffy coat derived. The apheresis donor was female and in the latter 2 cases the implicated donors were also both female and each contributed both plasma and buffy coats to the platelet pools. The other 3 cases with serological support were due to red cells in optimal additive solution (2) and cryoprecipitate (1). The donor in one of the cases associated with red cells in optimal additive solution had antibodies with specificity for HLA Class I antigens (A2 and B13) and also HLA Class II antigens (DR 4 and DR 53) all of which were expressed by the patient.

FFP alone or in combination with other components was suspected to have caused TRALI in 9 reported cases but none of these cases had proven donor white cell antibody with specificity for patient antigen. Seven of these cases were classed as unlikely to be TRALI, 1 as possible and 1 as probable. All the cases assessed as unlikely had no serological support for an immune basis for TRALI and all had other risk factors which could have caused their respiratory deterioration. The case assessed as possible TRALI had massive blood loss following infectious mononucleosis with splenic rupture, massive transfusion of blood and other fluids and a three-hour operation before respiratory deterioration. More than 60 donors contributed transfused components. Due to the scale and the presence of other risk factors for pulmonary damage the donors were not investigated. In the case which was assessed as probable the history was consistent with TRALI and a female FFP donor was found to have HLA Class I antibodies with 91% panel reactivity and HLA Class II antibodies specific for DR15 and 16 but a patient sample was not available for testing for concordance (see full case report below).

Figure 13

Components implicated in TRALI



Comparative results

In late 2003 the English National Blood Service (NBS), which provides more than 80% of UK blood components, introduced a policy of using male donors as far as possible to produce FFP and plasma for suspension of buffy coat derived platelet pools. Previously issued FFP from female donors was not withdrawn. In 2004, male donors provided 95% FFP units and 73% plasma for platelet pools in the NBS. In 2005, male donors provided 90% FFP and 84% plasma for platelet pools. Cryoprecipitate and apheresis platelets have continued to be obtained from similar numbers of male and female donors.

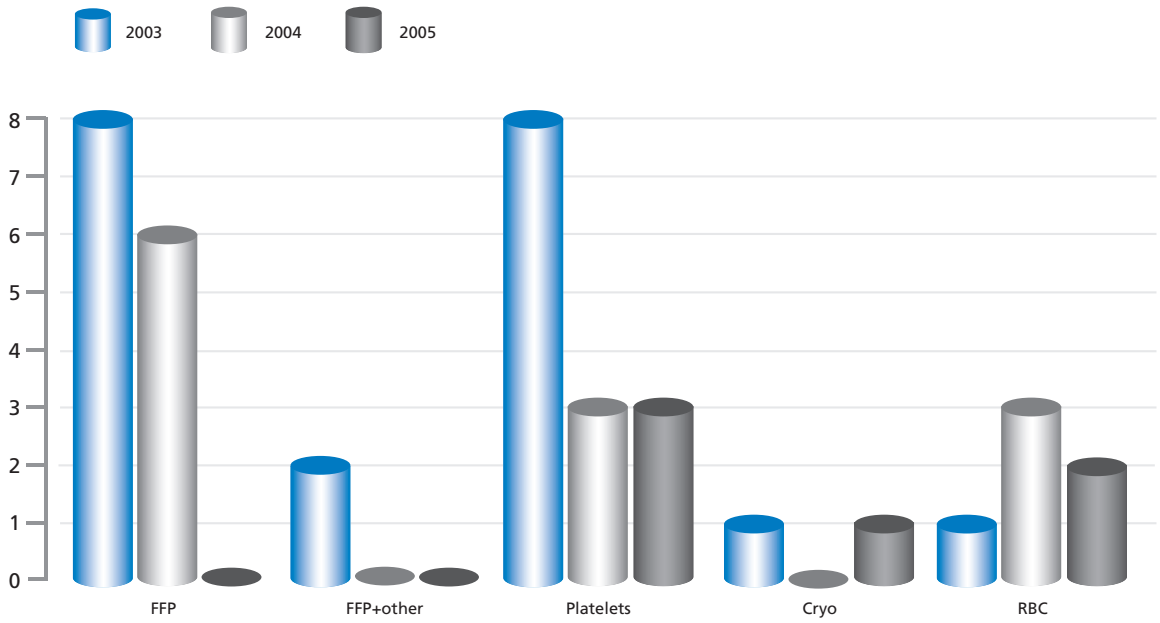
Comparison of TRALI reports in 2005 with those in previous years is presented to assess whether there have been changes in the observed pattern and incidence of TRALI related events since this change in practice. There are, however, several confounding factors which are relevant. These include: the long shelf life of FFP; significant delays from incident to return of SHOT TRALI questionnaires; an overall increase in the total number SHOT reports from 146 in 1996-1997 to more than 600 in 2005 and a new donor exclusion since April 2004 which applies to donors transfused since 1980. Finally, the assessment of the probability of TRALI in each case is a clinical judgement rather than an exact science.

Implicated components and donors

TRALI cases proven to involve a donor with leucocyte antibodies with specificity for patient antigen, have been analysed by implicated component in 2003, 2004 and 2005. Results are shown in Figure 13. Cases involving FFP with proven relevant antibody have dropped from 10 in 2003 to 6 in 2004 and none was identified in 2005. Cases involving platelets dropped from 8 in 2003 to 3 in 2004 and 3 in 2005. All cases with proven relevant antibody involved female donors.

Figure 14

Cases of TRALI with relevant donor antibody analysed by implicated component and by year 2003-2005



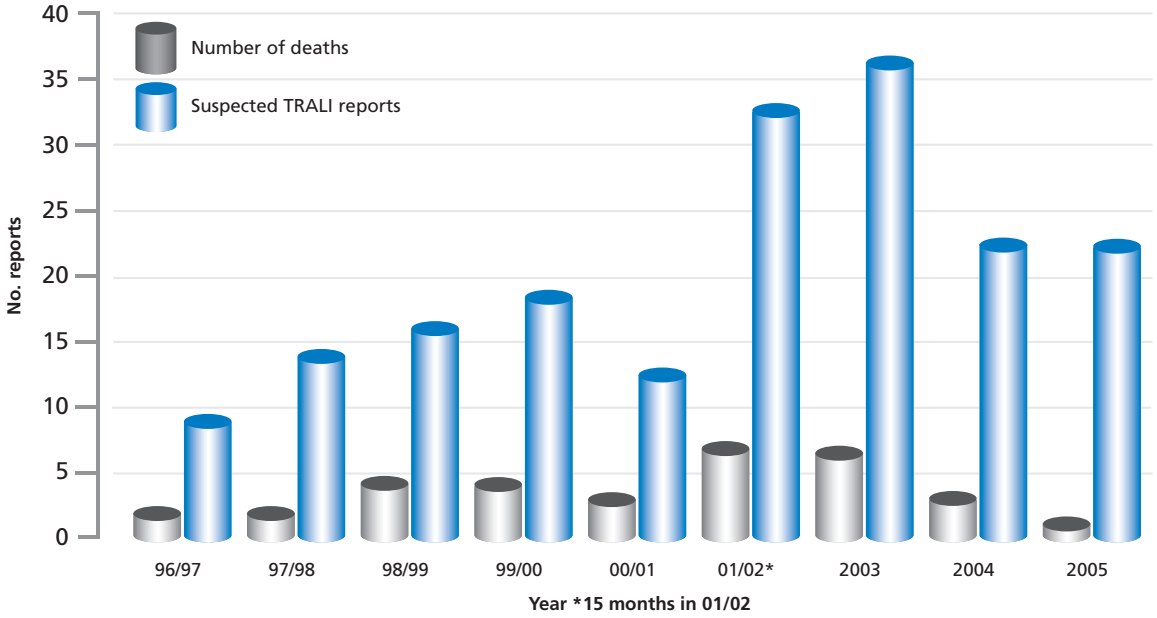
Deaths

The number of reported deaths at least possibly due to TRALI each year from 1996 to 2005 inclusive are shown on Figure 15. The total numbers of reports of suspected TRALI are also shown. Reports of suspected TRALI peaked in 2003 followed by a drop in 2004 and 2005. Reported deaths, at least possibly attributable to TRALI, showed a gradual increase from 2 in 1996/97 to 7 in 2003 followed by a decrease to 3 in 2004 and 2 in 2005.

The numbers of deaths over the past 3 years in cases classed as highly likely or probable TRALI were 4 of 22 cases in 2003 (cause of death possibly due to TRALI in 2 and likely to be related in 2). In 2004, 2 deaths occurred in 13 highly likely or probable TRALI cases of which 1 was likely to be related to TRALI and 1 was possibly related. In 2005 there has been 1 death in 6 patients in this group, this death was unrelated to TRALI.

Figure 15

Deaths at least possibly due to TRALI and number of TRALI reports analysed by year 1996-2005



Case histories

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

Case 5

A 17-year-old female was admitted as an emergency in December 2003 for treatment of a ruptured ectopic pregnancy with intra-abdominal bleeding. She had been previously fit and well. Her preoperative haemoglobin was 8.0g/dL and she was transfused with two units of red cells in optimal additive solution in theatre. The estimated intra-abdominal blood loss was 800 mLs. Within two hours of transfusion there was 'a dramatic deterioration in lung compliance and oxygenation. This was accompanied by frothy secretion in the endotracheal tube'. The reaction was not accompanied by fever, rigors, hypotension or hypercapnia and there were no clinical signs of heart failure. She was admitted to ICU and mechanical ventilation was required for the next 18 hours following which she made a full recovery. CXR following respiratory deterioration showed 'Bilateral perihilar and upper lobe air space shadowing'. Donor investigation identified that the female donor of one of the red cell units had HLA Class II antibody specific for DR1. The patient was DR1 positive. It was concluded that the case was highly likely to have been TRALI.

Case 19

A 40-year-old female underwent a radical hysterectomy for cervical cancer in June 2005. She had a postoperative bleed and was transfused with 4 units of red cells to replace blood loss and 4 units of FFP to correct coagulation abnormality. Almost immediately after completing transfusion of the final unit of FFP she became dyspnoeic and her oxygen saturation dropped to 60% on 100% oxygen. She required intubation, transfer to ICU and mechanical ventilation for 24 hours. Her chest x-ray showed 'pulmonary oedema' but there were no clinical signs of heart failure and diuretic treatment was not given. The reporter was 'certain' that her symptoms and signs were related to transfusion. Her clinical condition 'reversed relatively quickly' and she made a complete physical recovery. Investigation of the FFP donors revealed that 3 were untransfused males who were excluded from further testing. The donor of the final FFP unit was an untransfused female donor, who had been pregnant twice, 9 and 14 years previously. She was found to have HLA Class I antibodies with 91% panel reactive activity and also HLA Class II antibodies. Unfortunately, a sample from the patient was not provided at the time of the reaction and she has declined to provide one subsequently. This case was assessed as probable TRALI because of the clinical features of the reaction together with donor HLA antibody results which were likely to correlate with patient HLA Class I antigen. In the absence of a patient sample, this could not be proven.

Case 2

A 29-year-old female had a history of multiple hospital admissions with atonic bowel and several previous laparotomies. She was admitted in December 2003 with small bowel obstruction which required further laparotomy to free adhesions and jejunostomy. She was admitted to ICU post operatively due to inadequate respiratory effort with 'asthma' and was mechanically ventilated. On ICU there was a rapid drop in haemoglobin and she was transfused with 4 units of FFP transfused over an hour and a quarter to correct abnormal clotting related to 'impaired liver function' and 4 units of red cells over 8 hours. During the final red cell unit she became hypoxic with tachycardia and her CXR showed 'pulmonary oedema'. Fluid balance for the 9 hours before hypoxia was more than 600 mL positive and the reporters indicated possible fluid overload. The patient remained on a ventilator for 9 days and died subsequently. The reporter indicated that this death appeared to be due to transfusion but another cause could not be excluded. Donor investigation revealed no significant antibody, one female FFP donor had very weak anti HLA Class I and II antibodies which were considered to be of doubtful significance. The patient had HLA Class I antibodies with 95% panel reactivity and also had HLA Class II antibody specific for DR II but all the transfused components were leucocyte depleted so these antibodies were considered unlikely to be of relevance.

This case was assessed as unlikely to be TRALI because of possible circulatory overload and doubtful serology.

COMMENTARY

- TRALI cases assessed as highly likely/probable dropped from 22 in 2003 to 13 in 2004 and to 6 in 2005.

  Although numbers have decreased, TRALI remains a serious consequence of transfusion with six probable or highly likely cases this year.
- Two deaths were at least possibly related to TRALI; this is the lowest mortality since 1996.
- All cases were correctly referred to Blood Centres but occasionally the opportunity to send a patient sample was missed. In 4 reported cases investigation was incomplete due to missing donor or patient samples. Three reported cases were not investigated.
- Female donors were implicated in all cases in which a relevant leucocyte antibody was found (6). All such cases involved antibodies with HLA specificities. Granulocyte-specific antibodies were not proven to be implicated in any case.
- Platelets were the most commonly implicated component with proven relevant leucocyte antibodies this year (3 cases: 2 apheresis and 1 buffy coat derived). The number of cases of TRALI due to transfusion of platelets with donor leucocyte antibody proven to correspond with patient antigen decreased from 8 in 2003 to 4 in 2004 and 4 in 2005.
- No case of TRALI due to transfusion of FFP from a donor with leucocyte antibody proven to correspond with patient antigen was found this year. This contrasts with 8 such cases reported in 2003 and 6 in 2004, all from female FFP donors. It is probable that one case this year was caused by anti HLA in FFP from a female donor but patient testing was not possible to confirm this.
- It appears likely that the reductions observed in the number of TRALI reports, deaths and cases firmly implicating FFP and platelets in 2004 and 2005 relate to the policies of preferentially obtaining FFP and plasma for platelet pooling from male donors since late 2003 and the exclusion, since April 2004, of donors transfused since 1980.
- Two cases with proven serological support concerned transfusion of red cells in optimal additive solution, while 1 case involved cryoprecipitate. This suggests that as little as 30 mL of plasma can trigger a TRALI reaction.

RECOMMENDATIONS

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

  Action: HTTs.

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

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

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

  Action: Reference laboratories.

- UK Blood Services must continue to keep female contributions to FFP and plasma for platelet pools to an absolute minimum.

  Action: UK Blood Services.

- Further TRALI risk reduction might be achieved by preferential recruitment of male apheresis platelet donors, screening female platelet donors for leucocyte antibodies or by replacing part of the supernatant plasma with additive solution.

  Action: UK Blood Services.

10 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.

Three cases were reported as possible PTP of which two fulfilled the SHOT definition. Both of these are described below.

Case histories

Case 1

A 70 year old female was transfused uneventfully with 10 units of red cells, 3 platelet pools and 8 units of FFP during and after aortic and mitral valve replacement and coronary artery bypass graft. Her pre-operative platelet count was 208 x 10^9 /l and post-operative platelet count was 59 x 10^9 /l. Eight days after transfusion she developed a purpuric rash, bruising and a minor haemorrhage. Her platelet count at this stage was 3 x 10^9 /l and she did not respond to random donor platelet transfusion.

Investigation revealed that the patient had HPA-1a antibodies and her platelet genotype was HPA-1a negative. Enzyme-linked immunosorbent assay (ELISA) investigation for heparin/platelet factor 4 antibodies was negative. These results are consistent with a diagnosis of PTP due to anti-HPA-1a. She was treated with intravenous immunoglobulin and subsequently with HPA-1a negative platelets. Her thrombocytopenia was complicated by haemorrhagic pleural effusion.

She had had two pregnancies, the most recent being more than twenty years previously and had no history of neonatal alloimmune thrombocytopenia in either baby. She had not been transfused before this hospital admission. Platelet recovery to >50 x 10^9 /l occurred within 9 days and the patient made a full clinical recovery. The clinical picture and laboratory findings supported a diagnosis of PTP due to anti-HPA-1a.

Case 2

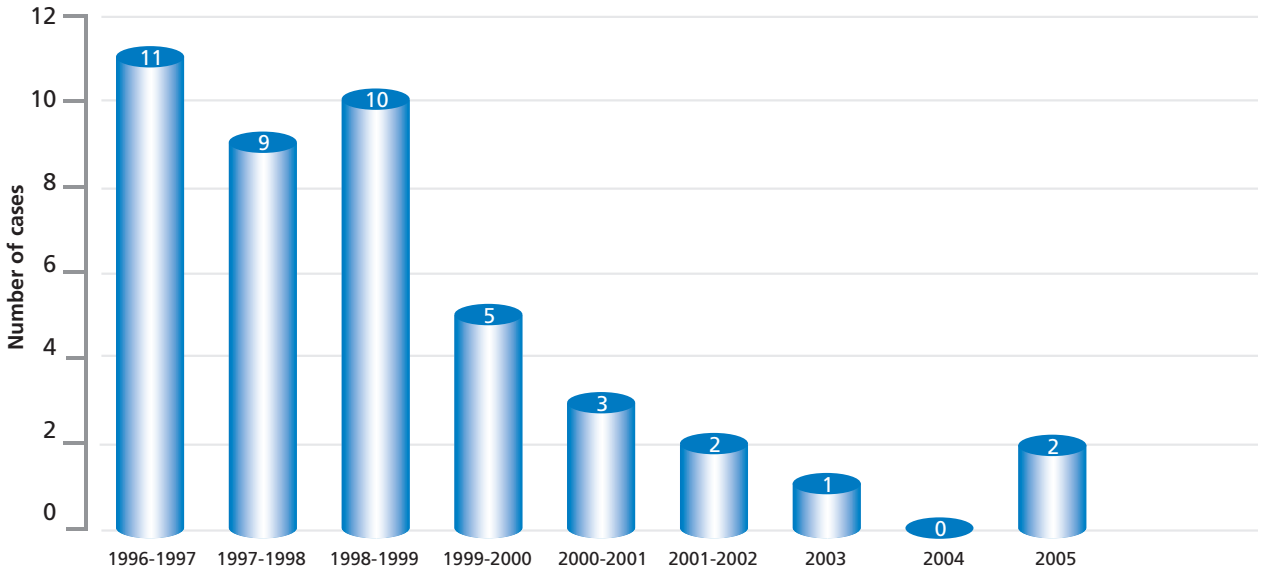
An 81 year old female underwent a right hemicolectomy for a tumour in the ascending colon. She was transfused uneventfully with 7 units of red cells pre and peri-operatively. Post-operatively she was given 2 units of FFP because of prolonged clotting times and one unit of platelets because her platelet count was 38 x 10^9 /l . Subsequent routine post-operative blood counts showed a platelet count of 99 x 10^9 /l on the 10th post-operative day and 5 x 10^9 /l on the 14th. She had a past history of an episode of thrombocytopenia in 1984 which responded to steroids. On that occasion, her platelet count was 13 x 10^9 /l and bone marrow aspirate indicated peripheral consumption. She later developed autoimmune hepatitis. The reporter initially thought ITP was the most likely reason for the recent episode reported to SHOT but felt PTP was possible given the recent history of transfusion. Investigation revealed pan-reactive platelet specific antibodies with a relative HPA-1a specificity. The patient's platelet genotype was HPA-1a negative. The laboratory report concluded that her results were consistent with post transfusion purpura. She had had a single pregnancy more than 20 years before and had been transfused more than 20 years previously. She was treated with intravenous immunoglobulin and steroids and her platelet count recovered to >50 x 10^9 /l in 4 days. This patient died subsequently of causes unrelated to thrombocytopenia. This case has been included as PTP due to anti-HPA-1a.

COMMENTARY

- Two cases of confirmed PTP were reported this year. The graph (Figure 16) shows the number of cases of confirmed PTP reported to SHOT each year since 1996. The drop in numbers of cases of PTP since the introduction of universal leucodepletion in 1999 has been maintained.

Figure 16

Number of cases of confirmed PTP reported to SHOT each year



- As well as a drop in the number of reported cases of PTP since the introduction of leucodepletion; there has also been a change in the transfusion profile before development of PTP. Before April 2000 all 29 patients, for whom components were recorded, had received red cell transfusion without platelet transfusion before PTP developed. After April 2000, 5 of 8 patients had received both RBC and platelet transfusion and 3 had received RBC alone.
- Both confirmed cases were female; this is consistent with previous years. Overall, including this year, there have been 43 cases of confirmed PTP reported since 1996. Of these, 42 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 has been identified in 36 of 43 (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 referral to a platelet reference laboratory for relevant investigation.

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

11 Transfusion Associated-Graft versus Host Disease

Definition (Updated 2005)

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

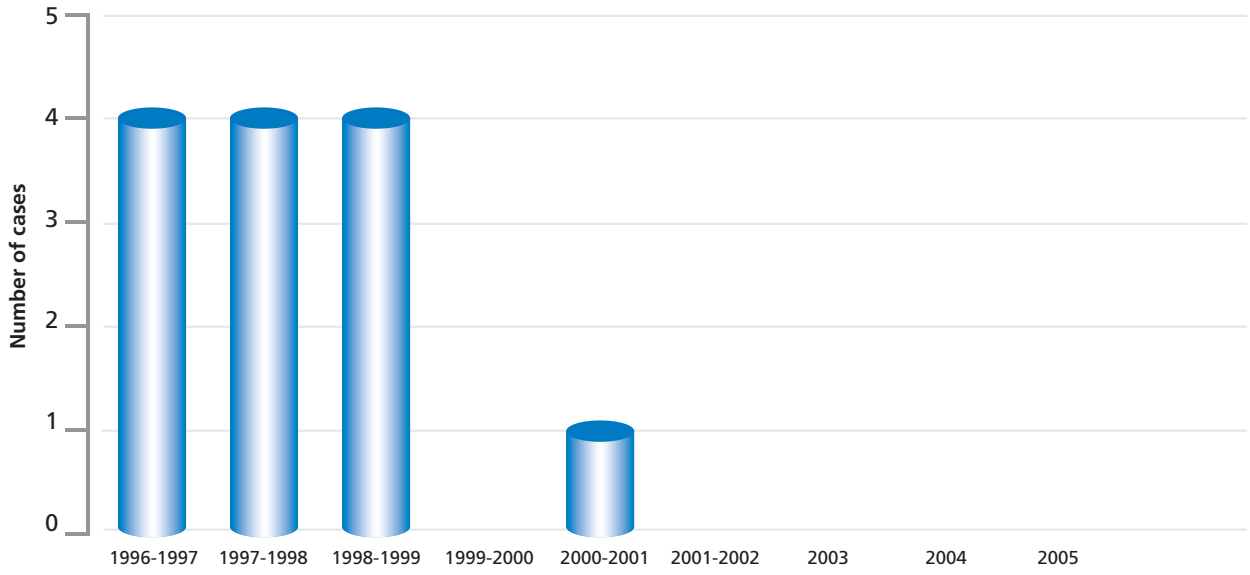
There were no new cases of TA-GvHD during this reporting period.

COMMENTARY

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

Figure 17

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



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 TA-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. [23]

One hundred and six patients who had a requirement to receive irradiated blood but who did not receive it are identified in the Chapter relating to IBCT (Chapter 5). Fortunately, none developed the condition.

RECOMMENDATIONS

- Gamma irradiation of blood components for those at risk of TA-GvHD remains essential. BCSH Blood Transfusion Task Force Guidelines[24] define groups requiring this prophylaxis.

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

- 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.

  Action: UK National and Regional Blood Transfusion Committees to facilitate and co-ordinate, Hospital CEOs to implement.

- 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: BCSH.

12 Transfusion Transmitted Infections

Definition

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

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

And, either

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

Or

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

Reports of suspected transfusion transmitted infections

Forty-six reports of suspected transfusion transmitted infections were made from blood centres throughout the UK (41 in England and Wales and 5 in Scotland) to the NBS/HPA Centre for Infection Surveillance during 2005. Three reports (1 HBV and 2 bacteria) were determined to be TTIs according to the above definition. Two reports were of predicted HAV transmissions. 40 cases were concluded as not transfusion transmitted infections (14 HBV, 6 hepatitis C (HCV), 1 dual HBV and HCV, 1 HTLV, 4 HIV and 14 bacteria). One case (HCV) is pending complete investigation. A further report was received from the Health Protection Agency of a clinical diagnosis of vCJD in a blood transfusion recipient. All UK blood centres contributed to the scheme.

Case report of transfusion transmitted hepatitis B

A previously hepatitis B surface antigen (HBsAg) negative donor was found to be positive after routine testing in August 2005. An archive sample of a donation made four months earlier was retested and found to be weakly positive for HBV deoxyribonucleic acid (DNA), but negative for all other HBV markers. The plasma from this donation had been discarded however the red cells had been transfused to a female recipient, aged 55 years following a gastro-intestinal haemorrhage. This recipient was tested and found to have evidence of a recently acquired hepatitis B infection: anti-HBV core IgM, anti-HBV core (HBc) and anti-HBV e-antigen (anti-HBe) positive and HBsAg and HBV DNA negative. The investigation concluded that the HBV infection in the recipient was due to an HBV infectious donation in the early acute phase of infection.

Case report of transfusion transmitted *Enterobacter cloacae*

One recipient (63 year old female) received four platelet units following a cerebral bleed due to chronic severe resistant ITP in March 2005. The first 3 units (two apheresis and one pooled platelets) were transfused without problems, however after transfusion of the fourth unit (3 day old pooled platelets) the recipient developed rigors, temperature, tachycardia and wheeze. *Enterobacter cloacae* was cultured from the patient and from the pooled platelet unit. All 4 donors were investigated: *Enterobacter cloacae* was not cultured from arm swabs from any of the donors. Blood and urine cultures from all four donors were also negative. The patient made a full recovery within 12 hours following treatment. The probable source of the recipient's reaction was concluded to be a unit of platelets contaminated with *Enterobacter cloacae*: no source of contamination was identified.

Case report of transfusion transmitted *Staphylococcus epidermidis*

One recipient (36 year old male) developed pyrexia and rigor following transfusion of a pooled platelet unit. Cultures from the implicated unit and the patient grew penicillin resistant *Staphylococcus epidermidis*. Molecular types of isolates from the pack and patient were indistinguishable using pulsed-field gel electrophoresis (PFGE). Four donors were recalled for arm swabbing and, although a number of staphylococci were grown, none of the donors was colonised with the identical strain of *S.epidermidis* found to be contaminating the pack. Skin flora can vary from day-to-day and there was a considerable gap between donation and swabbing, so a donor could not be ruled out as the possible source of contamination. Three related red cell units were recalled; all were free from contamination. The fourth red cell unit was transfused with no report of any adverse events. This case was concluded to be bacterial contamination with *S.epidermidis* of a pooled platelet unit, assumed but not proven to originate from the skin of one of the donors.

Reports of further incidents

Hepatitis A

1. In December 2005 the blood services were notified of a confirmed acute hepatitis A infection in a regular blood donor, who developed symptoms eight days following donation. The archive was tested by polymerase chain reaction (PCR) and found to be positive. The red cell unit was discarded, but the platelets had been used in a pooled platelet unit (suspended in plasma from another donor) and transfused to a female recipient 2 days after donation. Upon notification of the infection in the donor, the recipient was given passive and active immunisation, as per recommended guidelines[25] and tested for HAV. Traces of HAV antibodies were found, which may have been passive transfer from previous blood transfusions. A blood sample 3 months later from the recipient was HAV IgM positive, at a low level and there was a mild elevation in liver function tests. The conclusion of the investigation was that although transmission from a donor with confirmed hepatitis A was predicted, prompt immunisation appears to have prevented transmission or reduced the impact to sub-clinical levels with no sequelae.

2. In July 2005 a donor notified a blood centre that he had been clinically diagnosed with hepatitis A, 3 weeks after donation. The red cell component of this donation was discarded. The recipient of the platelets died of other causes, prior to testing for HAV. The FFP was transfused to a patient with alcoholic liver failure. When tested this recipient had evidence of immunity to HAV (HAV IgM negative, total HAV positive). This patient subsequently died. There was insufficient sample from the donor's index archive to test by PCR. A previous archive sample from the donor was HAV IgG negative. The donor has not responded to requests for additional samples and to date no serology for the donor has been seen by the blood services. The donor's record is flagged for HAV testing at their next attendance. This case is concluded to be a predicted potential transmission of hepatitis A, where the diagnosis in the donor was not confirmed and no transmission to any recipient was detected due to death or probable immunity.

vCJD

In early 2006 a further case of vCJD associated with a blood transfusion was reported. In 1997 a patient received a unit of non-leucodepleted red blood cells. The donor developed symptoms of vCJD about 20 months after donation and subsequently died. The recipient developed symptoms in 2005 and a clinical diagnosis of vCJD was made in early 2006. The recipient is a methionine homozygote at codon 129 of the prion protein gene. As the recipient is a UK resident, dietary exposure to bovine spongiform encephalopathy (BSE) cannot be excluded. The recipient was alive at the time of preparation of this report. (For more information on variant CJD see http://www.cjd.ed.ac.uk/).

Reports from previous years

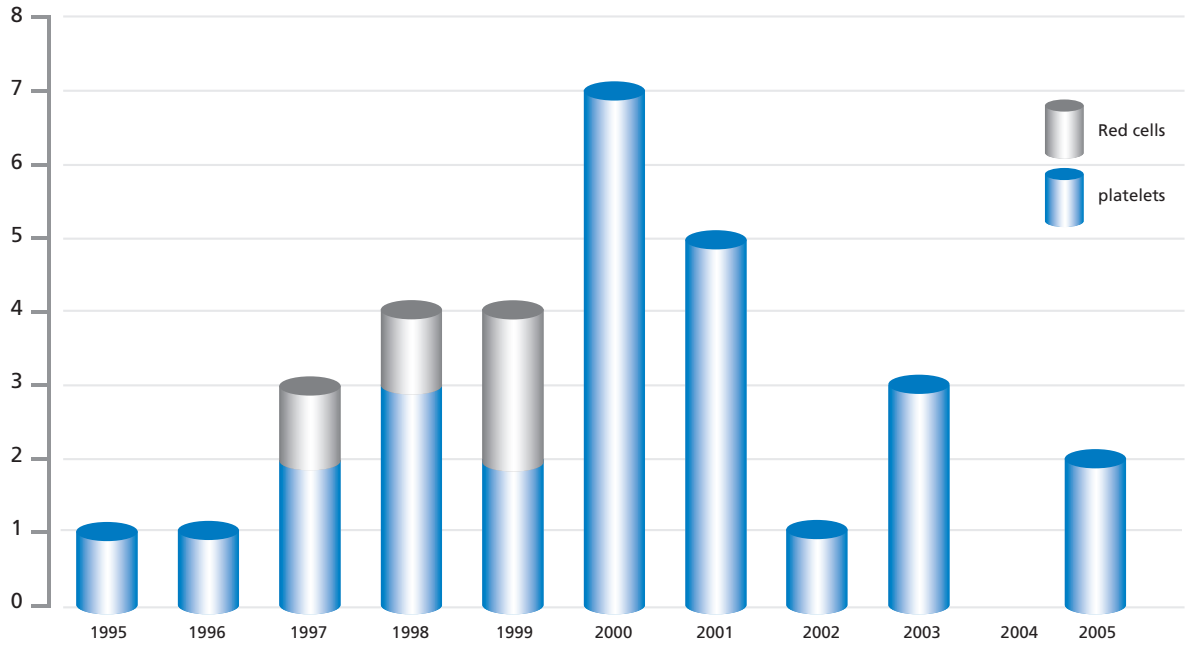
The case reported as pending in 2004 (HHV-8) is now nearing completion; all donors have been recalled and have provided blood samples for HHV-8 testing. Results will be reported when available.

Cumulative bacterial data

Since 1995, 31 cases of transfusion transmitted bacterial infection have been reported, of which 6 recipients died (Figure 18). The majority of these cases relate to platelet units (9 apheresis and 18 pooled). In 2004 there was a further incident involving contamination of a pooled platelet pack with *staphylococcus epidermidis*, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely (not included in figure 18).

Figure 18

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



Further cumulative data is available at http://www.hpa.org.uk/infections/topics_az/BIBD/menu.htm.

COMMENTARY

- For a case to be reported to this surveillance system, an infection must first be diagnosed, transfusion suspected as the means of acquisition/transmission, and this suspicion has to be communicated to the blood service. Under-ascertainment can be the result if omissions occur at any of these stages. Therefore surveillance of TTIs tends to be biased towards ascertainment of acute cases that are clinically apparent or investigation of newly acquired infection in returning blood donors. However, each year some infections among individuals who have received blood transfusion(s) in the past are reported to the blood services and investigated. All cases reported to the blood services have been reported to SHOT.
- Each year the number of reports received is small and fluctuations are to be expected. This year's findings are consistent with the current very low estimated risk of HIV, HCV and HBV infectious donations entering the UK blood supply.
- Notification from blood donors of infections that developed post donation enabled the blood service to identify two cases where transmission of HAV was predicted. Prompt action with passive and active immunisation to one recipient appears to have either prevented transmission or reduced the impact to sub-clinical levels. This emphasises the importance of blood donors notifying the blood service of infections detected after donation.
- The report of a third case of vCJD infection in a recipient of non-leucodepleted red blood cells provides further evidence that vCJD may be transmitted through blood transfusion. In all three cases the possibility that the recipient acquired infection through dietary exposure to BSE could not be ruled out. For the first reported case it was estimated that the chance of observing a case of vCJD in a recipient in the absence of TTI was about 1 in 15,000 to 1 in 30,000.[26] A number of precautions are in place to reduce the risk of transmission through blood transfusion. These include leucodepletion of blood components and the exclusion of candidate blood donors who have received transfusions since January 1st 1980 from donating blood.

- Although 16 cases suspected to be due to bacteria were reported and investigated during 2005, only two cases were confirmed. It is important that hospitals notify the blood services as soon as bacterial infection in a recipient is suspected and return the pack for complete investigation. The small number of confirmed bacterial cases seen in the past two years is encouraging and suggests that actions to reduce bacterial contamination, such as sample diversion pouches and enhanced donor arm cleansing, are effective.
- The Standing Advisory Committees (SAC) of the Joint UKBTS/NIBSC Professional Advisory 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, the SAC Transfusion Transmitted Infection (SACTTI) regularly reviews the residual risk of transfusion transmitted HCV, HIV and HBV infections to assess any need for additional testing methods, such as HIV RNA testing, HBV DNA or anti-HBc. The SAC Care and Selection of Donors ensures donor deferral criteria are optimal in terms of exclusion of donors with behaviour that may put them at increased risk of contracting transfusion transmissible infections.

RECOMMENDATIONS

- Hospitals should continue to report and investigate all possible incidents of post-transfusion infection appropriately and adequately.

  Action: HTTs.
- Donors should be reminded to report any infections developing post donation to their local blood centre.
- UK Blood Service collection teams should ensure donor selection guidelines are adhered to at all times in order to prevent transmission of blood borne infections.

  Action: UK Blood Services.
- Efforts to prevent bacterial contamination of blood components should continue. 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)[20] with regard to the visual inspection of blood components immediately prior to transfusion, to check for any irregular appearance.

  Action: UK Blood Services, hospital transfusion laboratories, staff undertaking pre-transfusion bedside checking.
- Hospitals should consult 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 or their residues and packs returned to the blood service for testing.

  Action: HTTs.

13 Acknowledgements

The Steering Group would like to take this opportunity to thank the following individuals and organisations for their contributions without which the publication of this ninth annual SHOT report would not have been possible.

The Blood Transfusion Services of the United Kingdom for funding and support

~~~~~~~~~~

The Royal College of Pathologists for their support and use of facilities

~~~~~~~~~~

Karen Carter - Marketing Services, NHSBT, for help and advice with the production of the report

~~~~~~~~~~

Kirk Beard - NHSBT, for the provision of data relating to the issue of blood components from the Transfusion Services of the UK

~~~~~~~~~~

Rob Hick & Judith Chapman- Blood Stocks Management Scheme, for the provision of data relating to the issue of blood components to hospitals in the UK

~~~~~~~~~~

Marcela Contreras, NHSBT, Neil Soni, Imperial College Medical School and Cliff Morgan, Royal Brompton Hospital for expert review of the TRALI cases

~~~~~~~~~~

Hazel Tinegate, Claire Thompson and colleagues in the Northern and Yorkshire regions for undertaking the "Where and When" study

~~~~~~~~~~

Clinical and Scientific staff, in hospitals and reference laboratories, who have contributed to the clinical and laboratory investigation of cases.

~~~~~~~~~~

Paul Ashford and Ceri Frampton - WBS, for maintenance of the SHOT website

~~~~~~~~~~

MHRA and Assad Afzal of Charles McKenzie Consulting for provision of the SABRE system and ongoing technical support

~~~~~~~~~~

Angela Allen, Personal Assistant to Dorothy Stainsby

~~~~~~~~~~

Christine Smith, Personal Assistant to Hannah Cohen

All hospitals who have participated in SHOT reporting

Without your support, SHOT would not be possible
~~~~~~~~~~

14 References

1 Asher D, Atterbury C L J, Chapman C et al, Serious Hazards of Transfusion Annual Report 2000/01, ISBN 0 9532 789 4 8, 9 April, 2002

2 Health Service Circular, Better Blood Transfusion - Appropriate Use of Blood, HSC 2002/009 04 July 2002

3 National Comparative Audit of Blood Transfusion
http://www.blood.co.uk/HOSPITALS/safe_use/clinical_audit/National_Comparative/index.asp

4 NPSA. Safer Practice Notice 14: Right patient, right blood. October 2006
A link to this document will be available on the SHOT website http://www.shot-uk.org as soon as possible

5 NPSA SPN on Safer Patient Identification 22nd November, 2005
http://www.npsa.nhs.uk/site/media/documents/1440_Safer_Patient_Identification_SPN.pdf

6 Blood Stocks Management Scheme
http://www.bloodstocks.co.uk/

7 The NHS Confederation / NPSA, Creating a virtuous circle, ISBN 185947 089 0, 2003

8 The Blood Safety and Quality Regulations 2005, ISBN 0110990412

9 British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for the use of fresh frozen plasma, cryoprecipitate and cryosupernatant: British Journal of Haematology 2004: 126, 11-28
www.bcshguidelines.com

10 British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines For The Use Of Platelet Transfusions. British Journal of Haematology 2003: 122, 10-23
www.bcshguidelines.com

11 Report of the Review of Pathology Services in England
http://www.dh.gov.uk/PublicationsAndStatistics/Publications/PublicationsPolicyAndGuidance/PublicationsPolicyAndGuidanceArticle/fs/en?CONTENT_ID=4137606&chk=J4t5ZX

12 The Handbook of Transfusion Medicine 4th edition
http://www.transfusionguidelines.org.uk/index.asp?Publication=H1&Section=9&pageid=8

13 SHOT Minimum standards for investigation of transfusion related adverse reactions
http://www.shotuk.org/standards4investigation.htm

14 Please ask, NPSA
http://www.npsa.nhs.uk/pleaseask/

15 Pregnancy - routine anti-D prophylaxis for rhesus negative women
http://www.nice.org.uk/page.aspx?o=TA41

16 Statutory Instrument 2003 No. 696, The Prescription Only Medicines (Human Use) Amendment Order 2003
http://www.opsi.gov.uk/si/si2003/20030696.htm

17 British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for blood grouping and antibody testing in pregnancy.
http://www.bcshguidelines.com/pdf/pregnancy_070606.pdf

18 Practical Transfusion Medicine 2nd Ed., 2005, Eds Murphy M, Pamphilon DH, Chapter 9, page 130

19 Laupacis A, Brown J, Costello B et al, Prevention of post-transfusion CMV in the era of universal WBC reduction: a consensus statement. Transfusion 2001; 41: 560-9

20 British Committee for Standards in Haematology Blood Transfusion Task Force. The administration of blood and blood components and the management of the transfused patient. Transfusion Medicine 1999, 9, 227-238
www.bcshguidelines.com

21 British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for compatibility procedures in blood transfusion laboratories. Transfusion Medicine, 2004, 14, 59-73
www.bcshguidelines.com

22 Baglin, T. P., Keeling, D. M. & Watson, H. G. (2006) Guidelines on oral anticoagulation (Warfarin): third edition - 2005 update. British Journal of Haematology 132 (3), 277-285.
www.bcshguidelines.com

23 Nollet, Kenneth E. & Holland, Paul V. (2003)
Toward a coalition against transfusion-associated GvHD. Transfusion 43 (12), 1655-1657.

24 British Committee for Standards in Haematology Blood Transfusion Task Force. Guidelines for gamma irradiation of blood components for the prevention of transfusion-associated graft-versus-host disease. Transfusion Medicine 1996; 6, 261-271
www.bcshguidelines.com

25 Crowcroft NS, Walsh B, Davison KL et al. Guidelines for the control of hepatitis A virus infection. Communicable Disease and Public Health, 2001. Vol 4(3);213-227.

26 Llewelyn CA, Hewitt PE, Knight RSG, et al. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet, 2004. 363; 417-421