SERIOUS HAZARDS OF TRANSFUSION

ANNUAL REPORT

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British Blood Transfusion Society, British Society for Haematology
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GLOSSARY OF TERMS

AIHA	Autoimmune haemolytic anaemia
ALL	Acute lymphocytic leukemia
ALT	Alanine Aminotransferase
AML	Acute Myeloid Leukaemia
ANC	Assistant National Co-ordinator
ARDS	Acute respiratory distress syndrome
ATR	Acute transfusion reaction
BBTS	British Blood Transfusion Society
BCSH	British Committee for Standards in Haematology
BMS	Biomedical scientist
CAT	Column agglutination technology
CDSC	Communicable Disease Surveillance Centre
CMO	Chief Medical Officer
CMV	Cytomegalovirus
CNST	Clinical Negligence Scheme for Trusts
CPAP	Continuous positive airways pressure
CVP	Central venous pressure
CXR	Chest X-Ray
DAT	Direct antiglobulin test
DHTR	Delayed haemolytic transfusion reaction
DTR	Delayed transfusion reaction
EC	European Commission
FBC	Full blood count
FFP	Fresh frozen plasma
HAV	Hepatitis A virus
HBV	Hepatitis B virus
HCV	Hepatitis C virus
HIV	Human Immunodeficiency virus
HLA	Human leucocyte antigen
HNA	Human neutrophil antigen
HPA	Human platelet antigen
HTC	Hospital Transfusion Committee
HTLV	Human T-cell leukaemia virus
IAT	Indirect antiglobulin test
IBCT	Incorrect blood component transfused
IBGRL	International Blood Group Reference Laboratory
ICU	Intensive care unit
INR	International normalised ratio
IVIgG	Intravenous immunoglobulin
LISS	Low ionic-strength saline
MHRA	Medicines and Healthcare Products Regulatory Authority

MLA	Medical laboratory assistant
MSBOS	Maximum surgical blood order schedule
MSBT	Microbiological Safety of Blood and Tissues for Transplantation
NAO	National Audit Office
NBA	National Blood Authority (England)
NBS	National Blood Service
NBTC	National Blood Transfusion Committee (England)
NBUG	National Blood Service User Group
NEQAS	National External Quality Assurance Scheme
NHL	Non-Hodgkin's lymphoma
NPSA	National Patient Safety Agency
OAS	Optimum Additive Solution
PT	Prothrombin time
PTI	Post-transfusion infection
PTP	Post-transfusion purpura
RCP	Royal College of Physicians
RNA	Ribonucleic acid
RTC	Regional Transfusion Committee
SCD	Sickle cell disease
SDFFP	Solvent-detergent fresh frozen plasma
SOP	Standard operating procedure
SPOT	Specialist practitioners of transfusion
TA-GVHD	Transfusion-associated graft-versus-host disease
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection
TTP	Thrombotic thrombocytopenia purpura
UKBTS	United Kingdom Blood Transfusion Services
vCJD	Variant Creutzfeldt-Jakob disease
WCC	White cell count
ZBUG	Zonal Blood User Group

1. FOREWORD: SHOT DATA SHOULD BE USED TO GUIDE BLOOD SAFETY POLICY

With this sixth annual report, the Serious Hazards of Transfusion (SHOT) confidential enquiry provides an increasingly authoritative analysis of serious transfusion complications in the UK. "Wrong blood transfusions" remain the most frequent transfusion hazard, 1045 events (64% of a total of 1630 analysable reports) over 6 years, with a further increase of 21% this year, even accounting for this year's unique extended reporting period (see chapter 2). These incidents have resulted in 15 deaths (5 definitely, 2 probably and 8 possibly due to transfusion) and 69 cases of major morbidity, for example necessitating Intensive Care Unit (ICU) admission.

The continuing increase in "wrong blood transfusion" incidents is likely to reflect increased user confidence and consequently increased event reporting, although a real increase in numbers of errors cannot be excluded. More importantly, it highlights that after 6 years of SHOT reports, there is no evidence that effective measures have been put in place to reduce the widespread problem of misidentification. The recommendations of the Health Service Circulars HSC 1998/224[1] and HSC 2002/009[2] are a sound basis for better blood transfusion practice. However, audit showed limited implementation of the former[3] and widespread application of the latter has so far been limited by lack of designated resource (appendix 9). Commissioners of healthcare (e.g. Primary Care Trusts and Strategic Health Authorities) should ensure that adequate resources are made available to hospitals to allow implementation of the recommendations in this report. They should take an active role in the setting and monitoring of quality standards for blood transfusion. SHOT strongly supports the new Information Technology working group of the Chief Medical Officer's (CMO) National Blood Transfusion Committee (NBTC) (chapter 7), that has the infrastructure to oversee the co-ordinated development and assessment of new technologies that could reduce transfusion error.

Participation in SHOT, as directed by HSC 2002/009[2] and in the earlier HSC 1998/224[1], has been maintained at a high level at 93% (92% last year). We believe that attainment of fullest value from participation in SHOT requires an open learning and improvement culture, in which individuals feel that they can safely report errors without fear of unjustified disciplinary action. The data from hospitals where the culture of reporting to SHOT is well established suggests that elsewhere there is still under-reporting. It is of concern that 50.5% (191/378) of 'participating' hospitals stated that they had seen no incidents, strongly suggesting that incidents are passing unrecognised or unreported. The confidential and anonymised nature of the SHOT scheme makes it difficult to place errors in the overall context of transfusion activity in the UK. To obtain accurate information on participation, from 1 January 2003 participation has been defined to include only those hospitals which submit completed reports and data has been collected by use of a confidential pin number which will be linked to the level of blood issues to hospitals. The lack of denominator data makes meaningful interpretation of, for example, 'out-of-hours' errors impossible, and, therefore, development of denominator data is a priority for the coming year.

Systematic reporting and analysis of "near miss" incidents, which are more numerous than those that lead to mis-transfusion, can provide an important early warning of serious problems. "Near miss" data are also a valuable source of information to evaluate improvements in transfusion practice, such as the application of new technologies. However, whilst "near miss" event reporting has increased it remains sub-optimal, with 709 reports from 41% of eligible hospitals (167 of 405). Evidence from the aviation industry indicates that an increased volume of air safety reports, within a "no fault" environment, is associated with a marked decrease in the number of "high risk" reports. This approach to risk reduction has the potential for successful application in the context of transfusion errors. Whilst many hospitals may be investigating "near-miss" incidents internally, we are losing opportunities to learn from each other if we fail to capture, share and learn from this information.

Transfusion-related acute lung injury (TRALI), with 103 cases of varying degrees of probability from 1630 reports over 6 years, is a major cause of transfusion-associated mortality and morbidity in the UK. This complication has caused 25 deaths (7 definitely, 4 probably and 14 possibly attributed to transfusion) and 67 cases of major morbidity. Appropriately, the NBTC recommendations on the sourcing and viral inactivation of fresh frozen plasma (FFP) have included consideration of TRALI prevention (chapter 7). Of note, FFP caused 21/48 acute transfusion reactions (chapter 12), with cumulative data over 6 years suggesting that acute transfusion reactions to FFP are about 4 times more frequent, proportional to the number of units transfused, than those due to red cells (chapter 6). There is a need for standard laboratory protocols for investigation of adverse transfusion reactions to ensure accurate diagnosis, and the recent National Blood Service (NBS) guidelines on the investigation and management of TRALI (appendix 11) will contribute to consistency of investigation. Open (i.e. non-anonymised) reporting of adverse events in which there has been no error would also improve accuracy

of analysis. FFP is often misused (see chapter 12) and it is timely that revised British Committee for Standards in Haematology (BCSH) guidelines on FFP usage are in preparation. Retrospective reporting and analysis is always fraught with difficulties, and SHOT aims, over the next 12 months, to implement structured case review which it is anticipated will improve the accuracy of data on immunological complications of transfusion.

The current report has highlighted that failure of communication of special transfusion requirements was frequently associated with adverse events particularly in patients who required shared care (chapters 10, 12 and 13). Establishment of procedures for adequate communication between clinical as well as laboratory teams are essential for such patients. The forthcoming BCSH guidelines on the avoidance of transfusion-associated graft-versus-host disease (TA-GVHD) include irradiation, but will also make recommendations on communication where there is shared care and include input from the Pharmacists/Pharmacologists Community.

For the first time, the SHOT report includes an analysis of adverse events in paediatric patients. Over 6 years a total of 141 of 1630 (8.7%) analysable reports related to children (chapter 18). A recurrent feature was evidence of a "knowledge gap" in laboratory staff and clinicians in relation to special needs of infants. This should be addressed.

It is pertinent to consider the impact on SHOT of the European Community Blood Directive 2002/98/EC, due to become legally binding in the UK. Article 15 of this Directive mandates "Member States shall ensure that there is a system in place to collect, collate, and transmit information about adverse reactions and events related to the collection, testing, processing, storage and distribution of blood and blood components to the competent authority"[4]. The Directive provides a minimum standard for reporting of adverse events of transfusion, but notably does not include any requirement to report incorrect blood component transfusion events, an integral part of haemovigilance.

One way to limit adverse transfusion events is to restrict the use of transfusion to situations in which it is, on the basis of the best available evidence, essential. Appropriate prescribing and use of blood components must therefore continue to be strenuously promoted. Available strategies to reduce the need for transfusion should be implemented wherever their use is supported by sound evidence and evaluated where more evidence is needed. Development and assessment of new technologies for blood conservation should be actively supported.

Sustained active participation in SHOT requires demonstration of its effectiveness. Each annual SHOT report contains a number of evidence-based recommendations, although SHOT has no power to insist that they be implemented, or to monitor compliance. Other organisations within UK healthcare have to pick up the SHOT findings and consider what actions to take, but there is no clear decision-making pathway for establishing priorities in blood safety. For the sixth consecutive year we recommend that there is a need for a national body, with relevant expertise and resource, to advise government on priorities for improvements in transfusion safety. SHOT data should be used to guide blood safety policy. With appropriate representation from the NBTC and SHOT on the Microbiological Safety of Blood and Tissues for Transplantation (MSBT) Committee, the resultant national body would have representation from all stakeholders involved in the blood transfusion process and sufficient relevant expertise to fulfill this extended remit.

Finally, SHOT gratefully acknowledges the commitment and enthusiasm of haematologists and allied professionals who take the time and trouble to complete SHOT questionnaires and are crucial to SHOT's continuing success.

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Chair, SHOT Steering Group.

2. MAIN FINDINGS AND RECOMMENDATIONS

SUMMARY OF MAIN FINDINGS

Change in reporting year

Hitherto the year end date for SHOT reporting has been 30th September. With effect from 2003 the reporting year becomes January to December in line with other major confidential enquiries. This report therefore covers a transitional period of 15 months, and data from October 2001 to December 2002 are included. Where comparisons are desirable with statistics from the previous report the figures are either quoted separately or are adjusted for the unequal time periods.

Participation and number of reports

In 2001 – 2002 378/405 (93%) eligible hospitals participated in the SHOT scheme, maintaining the high level of participation (92%) in the previous year. However the number of hospitals submitting reports fell slightly (187/405; 46%, compared with 48% last year). Nevertheless the overall number of reports received in the period from October 2001 to September 2002 (363) was increased by 15.2% compared with the preceding 12 month period, suggesting that reporting mechanisms are improving in the 'active' hospitals. An additional 115 reports were received between October and December 2002, making a total of 478 for the 15 month period.
It is of concern that 191/378 (50.5%) of 'participating' hospitals stated that they had seen no incidents, strongly suggesting that incidents are passing unrecognised or unreported.

Incorrect blood component transfused ("wrong blood") incidents

As in all previous years this category represents the highest proportion (71.7%) of all of reports received. For the 12 month period from October 2001 to September 2002, 258 new initial reports were received, and a total of 343 to the end of the new reporting year (December 2002), a 21.1% increase over the equivalent 12 month reporting period 2000-2001. This continuing steep rise in incorrect blood components transfused (IBCT) reports suggests a significant degree of underreporting in the past and increasing awareness and confidence in the SHOT scheme. A real increase in numbers of errors cannot however be excluded.
Multiple errors are a consistent feature of 'wrong blood' incidents and this year there were 552 errors in 346 fully analysed case reports, with multiple errors in 137 (40%) of cases. Errors continue to occur at all stages of the transfusion process; 149/552 (26.9%) errors in 134/346 (39%) of case reports occurred at the blood sampling, request and prescription stage; 157/552 (28.4%) errors in 120/346 (35%) of cases took place in the hospital transfusion laboratory; 236/552 (42.7%) errors in 159/346 (45.9%) case reports related to collection of blood from hospital storage sites and bedside administration. By far the most common error 103/552; (18.7%), was failure of the bedside checking procedure, which occurred in 30% of all IBCT cases.

Errors originating in the hospital transfusion laboratory may not be detectable further down the transfusion chain, whilst in other cases a correctly performed bedside check would have averted an incident. Of the 157 laboratory errors, 30 (25%) were grouping errors, 24 (20%) were errors in selection/issue of components, 23 (19.1%) were failure to access the patient's laboratory record, hence failing to meet special requirements. The remaining 80 errors, fully analysed in chapter 10, included sample transpositions, missed antibodies or incompatibilities, labelling and other clerical errors, failure to provide irradiated components and issue of outdated blood due to failure to clear satellite refrigerators.

The outcomes of errors reported this year were 32 instances of major ABO incompatible transfusion, resulting in 2 possibly transfusion-related deaths and 4 cases of major morbidity. There were 19 cases of RhD incompatibility (13/19 of these errors originated in the laboratory), of which 3 involved females of child-bearing potential, one of whom is known to have developed anti-D. Eighteen cases of other red cell antigen incompatibilities were reported, 1 of which led to major morbidity. Twenty one patients received unnecessary transfusions because of spurious full blood count (FBC) or coagulation screen results, possibly contributing to 2 deaths. Two patients suffered major morbidity due to ABO incompatible fresh frozen plasma (FFP) infusions.

In 83 cases special transfusion requirements were not met; 60 of these were patients at risk of transfusion-associated graft-versus-host disease who did not receive irradiated cellular components. A particular concern was poor communication, contributing to failures in 20 cases.

"Near-Miss" events

This year 146/405 hospitals (36%) reported "near-misses", an increase of 7% from last year. There was a 15% increase in numbers of reports received; 709 received in the 15 month extended reporting period and 519 in the 12 months to 30th September, 2002 compared with 452 last year. Again, sample errors were the largest group; 416/709 (59%), emphasising the risk of patient misidentification at an early stage in the transfusion process as well as at the end. Medical staff were implicated in 248/416 (59.6%) of these errors. There were 42 (6%) request errors, 87 (12%) errors in laboratory handling and/or testing and 91 cases (13%) of error in the selection, handling and storage of components, of which 27/91 related to incorrect storage in clinical areas resulting in wastage. Errors in component issue, transportation, collection from hospital storage sites and administration accounted for 73 (10%) of cases reported.

Reporting of "near-miss" events to SHOT is gaining momentum, but is still at a low level.

Immune complications of transfusion

There was a large increase in the number of reports of transfusion-related acute lung injury this year with a total of 33 completed reports, of which three were brought forward from last year, and four came between October and January i.e. the additional 3 months of reporting. There were thus 26 new cases in the 12-month period 01/10/01 to 30/09/02, compared with 15 in the corresponding period last year. The diagnosis of TRALI was considered to be highly likely or probable in 18/33 cases, whilst 14/33 were considered possibly TRALI and 1 unlikely.
The previously noted preponderance of patients with TRALI who were transfused because of haematological malignancy was not a feature this year, the majority of transfusions (14/33) being for surgical indications.

The majority of patients with TRALI (21/33) subsequently made a full recovery. One patient was reported to have recovered but with impaired respiratory function. Eleven patients died, 4/11 from their underlying condition whilst in 7/11 death was considered to be definitely (1), probably (2) or possibly (4) due to the transfusion. The diagnosis of TRALI in these 7 patients was highly likely in 1, probable in 2, possible in 4. Assessment of cases of TRALI, particularly retrospectively, is fraught with uncertainties, nevertheless with 7 deaths and 18 cases of major morbidity this year this is emerging as the most important serious complication of transfusion.

The component most commonly associated with the development of TRALI was FFP (12 cases) with a combination of components in 11 cases, platelets alone in 5 cases and red cells in 5 cases.

Forty-eight cases of acute transfusion reaction (ATR) were analysed; FFP, platelets or a combination of both were implicated in 31/48 and accounted for 27/34 (79%) of allergic or anaphylactic reactions. FFP continues to be used without good clinical indication. Cumulative data showed that acute transfusion reactions to FFP were 4 times more frequent, proportional to the number of units transfused, than those due to red cells (see chapter 6).

A newly recognised adverse reaction, that of transfusion-related neutropenia, was reported this year.

Delayed transfusion reactions (DTR) occurred in 47 patients, and were associated with 3 deaths, 2 definitely and 1 probably due to the transfusion. One further patient suffered severe morbidity. Kidd and/or Rhc antibodies were implicated in 75% of all cases and in all 3 deaths.

There were no new cases of transfusion-associated graft-versus-host disease this year, and only 3 cases of post-transfusion purpura (PTP), lending further support to the likelihood that quality controlled leucodepletion of all blood components, introduced by the UK Blood Services in 1999 may partially protect against these complications.

Transfusion-transmitted infections

Between 01/10/2001 and 31/12/2002, 34 post-transfusion infections (PTIs) were reported by blood centres in the UK, 20.9% fewer than in the previous year (43 reported between October 2000 and September 2001) despite the extended reporting period. Of these, 5/34 cases were confirmed as transfusion-transmitted infections (TTIs) due to bacterial contaminations; the remainder were considered not to have been caused by transfusion or

investigations were inconclusive. Two cases are still under investigation (1 Hepatitis B virus (HBV) and 1 Hepatitis C virus (HCV)).

All cases of TTI due to bacterial contamination were caused by platelets, which were 5 days old in 4/5 cases and 3 days old in 1/5. In 3/5 cases the implicated organism was *Staphylococcus epidermidis.* All 5 recipients had major morbidity, and none died.

Since infection surveillance began in 1995, bacterial contamination has accounted for 26/40 (65%) of TTI incidents affecting 26/43 (60.4%) of infected recipients and responsible for 6/7 deaths. Platelets were implicated in 22/26 cases and *Staphylococcus epidermidis* was isolated in 8/22 cases. The platelets were 3 or more days old in 21/22 cases.

The absence of any reports this year of transfusion transmitted HCV (or human immunodeficiency virus (HIV)) infections is consistent with the expected low risk of an HCV infectious donation entering the blood supply in the presence of the current testing of blood donations for both anti-HCV and HCV ribonucleic acid (RNA) (and anti-HIV).

GENERAL RECOMMENDATIONS

1. All institutions where blood transfusions are administered must participate in SHOT.

Participation in SHOT, already recommended by the UK health departments[1,2] will become a legal requirement when EC Directive 2002/98 on Safety of Human Blood[4] becomes UK law. SHOT, which is the UK Haemovigilance scheme, is a driving force for essential improvements in safety for patients who receive blood transfusions. Participation is an essential component of clinical quality and, as recommended by HSC 2002/009[2], should form part of assessment by regulatory bodies (the Commission for Health Improvement (CHI) and its successor in England and Wales and NHS Quality Improvement Scotland).

Reporting must be timely and should include notification of "near-misses" as well as serious adverse events related to blood transfusion. It is only by highlighting failures that we can learn from them and change unsafe practices. Whilst many hospitals may be investigating "near-miss" incidents internally, we are losing opportunities to learn from each other if we fail to capture, share and learn from this information.

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

Development of a culture in which the emphasis is on learning from errors in blood transfusion is key to participation in SHOT. Fear of criticism or disciplinary action and uncertainty about the consequences of reporting blood transfusion errors leads to underreporting. This results in lost opportunities to learn from errors and help staff to improve practice.

3. Adequate resources must be made available for improvements in transfusion safety in hospitals.

Commissioners of healthcare (e.g. Primary Care Trusts and Strategic Health Authorities) should ensure that adequate resources are made available to hospitals to allow implementation of the recommendations in this report. They should take an active role in the setting and monitoring of quality standards for blood transfusion.

4. Hospital transfusion teams must be established and supported.

As recommended in HSC 2002/009[2], hospitals involved in blood transfusion must establish and support a Transfusion Team. As a minimum this comprises a lead consultant in blood transfusion (with dedicated sessions), a hospital transfusion practitioner (nurse, biomedical scientist (BMS) or medical professional), and the blood bank manager. Chief executives should ensure that the team has full clerical, technical and IT support, and access to audit and training resources.

5. SHOT recommendations must be on the clinical governance agenda.

Hospital clinical governance committees must consider the recommendations contained in SHOT reports and determine an appropriate action plan for improving the safety of administration of blood components within their organisation.

6. Appropriate use of blood components must be strenuously promoted.

Appropriate use of blood is an integral part of any blood safety strategy and should be monitored by regular audit. Concise clinical guidance on the use of blood components is provided by the UK Blood Transfusion Services Joint Professional Advisory Committee and freely available on ***www.transfusionguidelines.org.uk*** and as the Handbook of Transfusion Medicine[5]. This guidance is revised in accordance with the current BCSH guidelines. There is a need for continued efforts to ensure that practitioners and patients have ready access to up-to-date, simple, consistent and user-friendly information on best practice.

The finding that 50% of IBCT events occur 'out-of-hours' should be of concern to all hospitals, and transfusions should only take place at night if clinically essential.

7. Training in blood administration should be implemented and competency testing developed to ensure an effective outcome.

The British Committee for Standards in Haematology guidelines on the administration of blood transfusion[6] provide a basis for training in blood handling.

All hospital staff who contribute to the transfusion chain must receive training in the procedures that they are required to undertake and their competency should be formally assessed and recorded.

Professional organisations should work towards development of a nationally accepted and validated system of competency testing for staff involved in the handling and administration of blood components.

8. Blood transfusion should only be prescribed by authorized clinicians.

Blood transfusion should only be prescribed by clinicians who have been authorized by the Trust following appropriate training.

9. Blood transfusion teaching must be included in all relevant academic curricula.

Teaching on blood transfusion safety must be a formal and required part of nursing and medical undergraduate courses and biomedical scientist training. Blood transfusion medicine, best practice and blood safety should be included in the curriculum for medical professional examinations.

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

This year about 35% of blood transfusion errors originated in the laboratory and 31.2% of laboratory errors occurred 'out-of-hours' when laboratory staffing may be sub-optimal. Hospitals must ensure that blood transfusion laboratories have adequate numbers of appropriately trained biomedical scientists to cover the 24-hour working day, including a core of permanent blood transfusion laboratory staff.

Standard-setting bodies need to develop standards for laboratory staffing, both within and outside normal working hours, taking into account external pressures such as the requirement for a 4 hour patient turnaround in A & E. Inspection for laboratory accreditation should include the quality of all aspects of the service including 'out-of-hours'.

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

Information technology has enormous potential to reduce the risk of transfusion errors. However, a co-ordinated approach to the development / assessment of new technologies is needed to ensure quality and "connectability" with other key systems used in the hospital such as patient administration systems, electronic records and systems used in Pharmacy and other clinical areas where positive patient ID is critical. This should be organised at national level. The Chief Medical Officer's National Transfusion Committee in England has recently set up an IT Working Group whose first objective is to bring together the disparate agencies and projects developing clinical IT systems in the NHS. New technologies have the potential to overcome inevitable human error but need to be developed and tested in "real life" clinical environments to demonstrate their true value.

- **Electronic positive patient/blood component identification "from vein to vein"** using readily available barcode technology and wireless hand-held scanners is already undergoing field trials in the UK. In addition to improving transfusion safety, this technology has many other potential applications in the clinical setting which should increase its affordability. The same electronic ID systems could be used to reduce prescribing and drug administration errors (a considerably greater cause of morbidity and mortality than transfusion errors) and ensure correct attribution of pathology results, dietary regimens and surgical procedures. A coordinated approach is essential to avoid the nightmare scenario of multiple, incompatible, bespoke systems for transfusion, pharmacy, pathology etc in each clinical area.

- **Automated laboratory equipment** with electronic interfacing reduces the risk of manual transcription and transposition errors but should complement, not replace, skilled and experienced staff.
- **Electronic issue of blood from the laboratory without conventional serological "crossmatching"** has the potential to improve blood utilization within a hospital and allow laboratories to meet increasing clinical workloads whilst maintaining patient safety. However, secure sample identification and recording of blood group/antibody screen results are absolutely essential. Ideally, electronic sample ID and a high level of automated testing, with electronic data transfer, should be used in laboratories using "electronic issue". The standards and specifications of such systems should be clearly defined in authoritative national guidelines which are regularly reviewed to keep up-to-date with technical developments.
- **Electronic control of the release of blood components from Blood Banks and satellite refrigerators** can improve patient safety and ensure the traceability of blood units. Computer controlled systems with positive patient and product ID, preferably based on barcode reading, can protect patients from one of the most common causes of mismatch transfusion errors identified in sequential SHOT Reports – collecting the wrong unit from the refrigerator. These systems can also monitor the location and storage status of blood throughout the hospital and improve the traceability of blood as required by the new EU directive. They will be particularly valuable where a central blood bank serves several geographically remote sites or a large number of satellite refrigerators. Once again, these systems should be developed and tested in routine clinical practice to ensure utility and robustness under normal working conditions.

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

Each SHOT report contains specific recommendations. However SHOT has no authority over implementation and cannot monitor compliance. Decision-making pathways are needed to enable data from SHOT to influence blood safety policy.
Bodies which support research, development and health technology assessment should consider blood safety and alternatives to transfusion when setting their funding priorities.

13. Poor communication is an important cause of adverse events.

Clear policies must be developed for communicating special transfusion needs of patients to other hospitals or units which may share their care, so as to ensure that all pertinent transfusion history is available. This is particularly relevant to peripheral blood and bone marrow stem cell transplant recipients. Active involvement of patients in this aspect of their care could reduce the frequency of errors and adverse reactions.
Increasing use of fludarabine means that many more patients are susceptible to TA-GVHD. Pharmacy departments should play a role in notifying patients and hospital blood banks when this therapy is commenced. The forthcoming BCSH guidelines on the avoidance of Transfusion Associated GVHD (which extend the current guidelines for irradiation[7]) include advice on communication where there is shared care and include input from the Pharmacists/Pharmacologists community.

SPECIFIC RECOMMENDATIONS

Incorrect blood component transfused

- **SHOT recommendations should be used locally to support risk management, clinical governance and education.**

    - In order for patients and staff to derive full benefit from the SHOT scheme, local initiatives to disseminate the main messages of the SHOT report are essential. These could form part of induction sessions for all staff groups or be regular sessions at hospital "Grand Rounds" or departmental training programmes.
    - Reporting should be the norm and full investigation of reported incidents should be carried out by individuals who are familiar with good practice guidelines for transfusion. SHOT findings should be part of mandatory training for all staff involved in the transfusion process.
    - All staff should be made aware through the Risk Management Committee of transfusion errors occurring in their department and in other departments within the hospital. This should not reveal the identities of individuals concerned, the emphasis being on avoiding repetition of errors and

encouraging staff to analyse their working practices to identify potential "weak links" which can be remedied.

- **Improved training of midwives in relation to anti-D administration is necessary**.
    - There is increasing risk of mis-administration with the rolling out of the routine antenatal prophylaxis programme. More secure and explicit communication of antenatal and postnatal results is required.
- **Human error in relation to patient identification is still the commonest problem leading to wrong-blood-in-patient.**
    - Educational initiatives have been inadequate in resolving this problem. Patients should be empowered to be involved in the bedside checking procedure.
    - Investment in the development and evaluation of technological solutions is essential if errors in the transfusion process are to be significantly reduced.

"Near-Miss" events

- Patients should wherever possible be educated about their own special transfusion requirements.
- Hospital protocols must state that there are no exceptions to the requirement for identity wristbands to be worn by all patients.
- As recommended last year, all hospitals must have a training programme in place for phlebotomy which must include medical staff.

Immunological complications

- **Patients receiving transfusion must be monitored.**
    - Patients receiving any blood component must be monitored to detect an acute reaction. Patients must be checked prior to the transfusion of each component and 15 minutes after its commencement.
- **Reduction of the risk of TRALI demands a high priority.**
    - Hospitals should continue to be aware of TRALI and to investigate and report possible cases. Continued education of all staff about this condition is encouraged so that cases may be investigated appropriately and implicated donors withdrawn.
    - Following evaluation of available options (e.g. sourcing of FFP from untransfused male donors, suspension of platelets in plasma-free medium), UK Transfusion Services should take all steps possible to reduce the risk of TRALI from blood components.
- **All adverse reactions should be fully investigated and reviewed.**
    - Analysis of cases of acute transfusion reaction and TRALI was unsatisfactory as many cases were not fully investigated and clinical details were sketchy. It is recommended that there is early evaluation of cases by the consultant(s) involved. A team approach including the haematologist and chest physician and/or ICU consultant may be helpful. The blood services are refining the algorithm for investigation of TRALI so the laboratory work-up of cases should in future be more consistent and complete (appendix 11).
    - Patients who have had a severe allergic reaction (anaphylactic/anaphylactoid) should be investigated for IgA deficiency.
    - There is a need for a guideline dealing with the investigation of all acute transfusion reactions.
    - A system of open, non-anonymised reporting to SHOT and specialist review of cases would improve evaluation of the risk of TRALI and should be developed.

- **FFP continues to be associated with significant risks of reactions including TRALI.**
  - FFP should only be used when clinically indicated in accordance with BCSH guidelines[8]. It is particularly important that guidelines for the management of high International Normalised Ratios (INRs) due to warfarin therapy are also followed[9].
  - There is continued evidence of inappropriate use of clinical FFP[10], and further local audits and educational programmes should be encouraged. A revised BCSH guideline is expected during 2003; in the meantime, existing BCSH guidelines[8,9] should be followed.
- **Particular care should be taken when providing blood for patients with a positive direct antiglobulin test (DAT), who are known to have an autoimmune haemolytic anaemia or have been recently transfused.**
  - Referral to a reference centre, if time allows, should be considered.
  - Where plasma samples are routinely used for pre-transfusion testing, it is recommended that serum samples are also used in the investigation of suspected transfusion reactions.
- **Suspected delayed haemolytic transfusion reaction (DHTR) should be carefully investigated.**
  - Investigation should include retesting of the pre-transfusion sample by different or more sensitive techniques. This may involve referral to a reference centre.
  - Serum (+ plasma if used routinely) should preferentially be used, to give maximum potential for identifying all antibody specificities present, including weak complement binding antibodies.
- **Patients with sickle cell disease (SCD) should be phenotyped prior to transfusion and blood selected for Rh and K.**
- **Automated systems or changes to indirect antiglobulin test (IAT) technology should be validated using a range of weak antibodies to ensure appropriate sensitivity.**
- **Information on previous transfusion history must be available to all who need it.**
  - Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies. These should be accompanied by information leaflets explaining the significance of the antibody and impressing that the card should be shown in the event of a hospital admission or pre-operative assessment.
  - When the care of patients with haematological disorders requiring transfusion support is shared, there is a risk that not all pertinent transfusion history will be available to both sites. In the absence of networked pathology information systems, it is essential that local procedures are devised for adequate communication.
- **Withholding transfusion may be a greater risk than DTR.**
  - When the laboratory cannot supply compatible red cells within the time-frame requested, there should be communication between the haematologist and the responsible clinician to determine whether the risk of delaying the transfusion outweighs the risk of a transfusion reaction and whether potentially incompatible red cells should be given.
- **No cases of TA-GVHD this year, but risk remains of this fatal consequence of transfusion.**
  - Despite the lack of cases this year, hospitals should remain aware of TA-GVHD and should be rigorous in putting systems in place to ensure that all patients at risk receive gamma irradiated products.
  - Products where partial haplotype sharing is likely should be irradiated. If donor lymphocytes are homozygous for one of the patient's haplotypes the donor lymphocytes can survive. Because they do not share the other haplotype of the patient, however, they can recognise the patient as foreign and set up a GVHD reaction. This is particularly likely to happen if human leucocyte antigen (HLA) matched

products or products from family members are used and for this reason these products should always be irradiated.
- New chemo- or immuno- therapeutic regimes should be assessed for their potential to cause susceptibility to TA-GVHD and guidelines modified accordingly.

- **PTP is a rare but treatable consequence of transfusion.**

  - Clinicians should remain aware of this rare but treatable consequence of transfusion. The mainstay of treatment is high dose intravenous gammaglobulins +/- steroids, with random (i.e. unmatched) blood components given only if there is significant bleeding.
  - If PTP is suspected, there should be urgent liaison with a reference laboratory for appropriate specialist investigation.
  - PTP is induced by a re-exposure to human platelet antigen (HPA) antigen in individuals with a history of previous immunising events. PTP can therefore occur following transfusion with any platelet-containing product. Now that leucodepletion removes most platelets from red cell components it may be that the classic picture of PTP occurring after red cell transfusion will change and we will see proportionately more cases following platelet transfusion. Non-classical cases should be reported to SHOT.
  - Patients with HPA antibodies should have appropriate antigen-negative cellular products if they require transfusion in the future. Screening should be offered to female relatives of child-bearing potential to see if they are at risk of forming antibodies capable of causing fetal/neonatal alloimmune thrombocytopenia. For HPA-1a this would include HLA typing for HLA DR 101 to identify those who are likely to form antibodies.

- **Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components.**

  - These include implementation of diversion of the first few mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site) and improvements in cleansing of donors' arms. Methods for testing platelets for bacterial contamination should be evaluated.
  - The risk of transfusion of a contaminated component can be reduced by adherence to BCSH guidelines[6] with regard to the visual inspection of units for any irregular appearance immediately prior to transfusion (particularly platelets).
  - Hospitals should consult the blood service about the investigation of transfusion reactions suspected to be due to bacteria. National guidance on the investigation of these cases is available from all NBS centres. Cases that are inconclusive due to discard of the implicated pack before sampling continue to be reported, therefore particular attention should be paid to the sampling and storage of implicated units.

- **Neonates and children are a vulnerable group with special transfusion requirements.**

  - Laboratory, nursing and medical staff should all be aware of the special considerations of component selection and/or manipulation for neonatal transfusion[11, 12].
  - The wearing and checking of patient identification is essential in the paediatric age group, who may not be able to identify themselves verbally.
  - Children receiving blood components should be closely monitored.
  - BCSH guidelines are as applicable to children as to adults and should be followed.
  - Paediatricians should be encouraged to report suspected transfusion-related adverse events and to disseminate lessons learned.

3. AIMS, EDUCATIONAL ACTIVITIES AND PUBLICATIONS

Aims. The Serious Hazards of Transfusion (SHOT) scheme was launched in November 1996. SHOT is a voluntary anonymised system which aims to collect data on serious adverse events of transfusion of blood components, and to make recommendations to improve transfusion safety.

Through the participating Royal Colleges and professional bodies, SHOT findings can be used to:

◊ inform policy within transfusion services
◊ improve standards of hospital transfusion practice
◊ aid production of clinical guidelines for the use of blood components
◊ educate users on transfusion hazards and their prevention

Educational Activities. SHOT findings continue to stimulate widespread interest in the UK and abroad. The following is a list of national and international meetings during 2001 and 2002 at which members of the SHOT team have presented results from the reports in the context of a broader view of transfusion safety.

2001

March	• SHOT Annual launch, London, UK
April	• British Society for Haematology Annual Scientific Meeting: invited lecture and oral presentation, Harrogate, UK • RCN Blood Transfusion Nursing Forum, Manchester, UK
May	• Baxter Symposium “El impacto clinico de la calidad total en el proceso de la medicina transfusional”, Merida, Mexico • Conference “Hematología 2001”, Havana, Cuba
June	• Adverse effects of blood products, AAGBI Workshop, Cambridge, UK • Postgraduate Haematology Course, London, UK • Association of Clinical Anaesthetists Update, London, UK • Interrelación entre Centros de Transfusión y Bancos de Sangre, Madrid, Spain
July	• ISBT Congress, Paris, France
September	• BBTS, Leeds, UK • CNST Update Seminar, London, UK • CMO conference on Better Blood Transfusion 2, London, UK • Hemovigilancia, Lima, Peru
November	• Plenary lecture on Haemovigilance and co-chair, ISBT Regional Congress, Shanghai, People´s Republic of China • Risk 2001, London, UK • CNST Update Seminar, Manchester, UK • Transfusion Medicine meeting, London, UK
December	• Workshop on haemovigilance, Sao Paulo, Brazil • Workshop on European Haemovigilance, Athens, Greece

2002

April	• BSH 42nd Annual Scientific Meeting, Brighton, UK
May	• DBTS / Sanguin Research Symposium, Amsterdam, Netherlands
June	• EHA 7th congress Florence, Italy • SHOT Presentation, University of the West Indies, Kingston, Jamaica
July	• SHOT Annual launch, London, UK
August	• ISBT, Vancouver, Canada
September	• HSANZ, ASM / ASBT, Adelaide, Australia • BBTS 20th Annual Meeting, Edinburgh, Scotland
October	• National Association of Theatre Nurses Conference, Harrogate, UK • NBS Clinical Audit Conference, Birmingham, UK • RCN Haematology and BMT Forum, London, UK • Sysmex User Symposium, Wishaw, UK
November	• ESTM, Bulgaria • Royal College of Anaesthetists and Association of Anaesthetists of Great Britain and Ireland Study Day , London, UK • 'My Own Blood' Symposium, Gothenburg, Sweden
December	• ESTM, Slovenia • Safety of Blood Components Conference, Naples, Italy • EHN 4th Seminar and 5th Hellenic Meeting, Athens, Greece

Publications 2001

Haemovigilance in the UK: 4 years of the SHOT scheme (oral), ISBT Paris July 2001, Transfusion Clinique et Biologique, 2001, 8 Supp 1, S23-005

EM Love, H Jones, LM Williamson et al, Haemovigilance and experience of the Serious hazards of Transfusion (SHOT) scheme in the United Kingdom (UK), Chinese Journal of Blood Transfusion 2001, 14, Supp: 19-23

Publications 2002

Williamson LM. Transfusion hazard reporting: powerful data, but do we know how best to use it? Transfusion 2002; 42: 1249-1252

Love EM, Jones H, Williamson LM, Cohen H, Todd A, Soldan K, Revill J, Norfolk DR, Barbara J, Atterbury CLJ, Asher D, Chapman C, SHOT – A voluntary system for the reporting of serious hazards of transfusion in the UK. TATM 2003; 5 (1): 249-255

4. OVERALL ORGANISATION AND REPORTING SYSTEM

Organisation

The strategic direction of SHOT comes from a Steering Group with wide representation from Royal Colleges and professional bodies representing medical, nursing and laboratory staff as well as Health Service Managers. The operational aspects of the scheme are the responsibility of a Standing Working Group, which is accountable to the Steering Group. The Terms of Reference of the Steering and Standing Working Groups, along with the current membership, can be found in appendix 1. Two national co-ordinators are responsible for receiving and collating reports.

Minutes of Steering Group meetings are sent to the Department of Health for information.

In the first three years funding was provided by the blood services of the United Kingdom and the Republic of Ireland supported by generous grants from the British Society for Haematology and the British Blood Transfusion Society (BBTS). From year 4 it was agreed that future financial support for SHOT would be provided by the four United Kingdom Blood Transfusion Services (UKBTS) on a pro-rata basis according to the number of red cells units issued.

SHOT was affiliated to the Royal College of Pathologists in November 1997.

Scope and Reporting System

Participation in the scheme is entirely voluntary. National Health Service and private hospitals in the United Kingdom as well as public hospitals in Guernsey, Jersey and the Isle of Man are invited to report. The Republic of Ireland also contributed reports up to and including the 1998/1999 report after which it launched its own haemovigilance scheme.

SHOT invites reports of major adverse events surrounding the transfusion of single or small pool blood components supplied by Blood Centres (red cells, platelets, FFP, methylene blue FFP and cryoprecipitate). It does not cover complications of fractionated plasma products (coagulation factors, albumin, immunoglobulin); as licensed medicinal products, these are already covered by the 'Yellow Card' system of the Medicines and Healthcare Products Regulatory Authority. (MHRA). Cases in which Anti D immunoglobulin is administered to the wrong patient, however, are reported under the category of Incorrect Blood Component Transfused. Adverse reactions to solvent-detergent treated fresh frozen plasma (SDFFP) are covered by the "yellow card" scheme. However, for purposes of comparison, complications of treatment with SDFFP should also be reported to SHOT.

During the period covered by this report, hospitals have been asked to report the following categories of adverse event:-

1. incorrect blood component transfused
2. acute transfusion reaction
3. delayed transfusion reaction
4. transfusion-associated graft-versus-host-disease
5. transfusion-related acute lung injury
6. post-transfusion purpura
7. bacterial contamination
8. post transfusion viral infection
9. other post-transfusion infection e.g. malaria
10. autologous pre-donation incidents
11. "near miss" events

Reporting of transfusion-transmitted infections

Suspected cases of TTI are reported, using local procedures, to supplying blood centres. Blood centre involvement is essential to ensure rapid withdrawal of other implicated components and appropriate donor follow-up. These cases are then reported by blood centres to the National Blood Authority/Health Protection Agency Communicable Disease Surveillance Centre (NBA/CDSC) post-transfusion infection surveillance system. If the SHOT office is notified directly of an infectious hazard, the hospital haematologist or biomedical scientist (BMS) who reported the incident is approached by the SHOT office to ensure that all relevant personnel have been informed and that the incident has been reported to NBA/CDSC. In Scotland reporting of suspected and confirmed incidents of TTI is managed through the Regional Transfusion Centres with information being collated by the National Microbiological Reference Unit. Details of numbers and types of incidents thus reported are provided to NBA/CDSC on an annual basis for the purpose of inclusion in the SHOT report.

Reporting of non-infectious adverse events

At hospital level, these are generally reported to the local clinician responsible for transfusion, usually a consultant haematologist. The incident is then notified to the SHOT office on the yellow 'initial report' form. For some complications, the local blood centre will have been involved in the investigation of the case. On receipt of a report, the assistant national co-ordinator allocates a number to the case, then issues a detailed follow-up questionnaire specifically designed for each hazard.

This enables confidential discussion of an incident between the SHOT office and the reporter if necessary. When incomplete information is received or when some clarification is needed, the SHOT staff approach the local contact named on the report form. Once complete, the information in the questionnaire is entered in an anonymised way on to the SHOT database.

The SHOT staff may offer to visit the reporting clinician, to assist with the completion of the questionnaire.

Reporting of "Near Miss" Events

Following 2 earlier successful pilots, all hospitals eligible to report full incidents are now encouraged to report "near miss" events. The questionnaires which cover this type of incident are shorter and less complex than those designed for full incidents. However, in order to ensure consistency in all types of reporting, "near miss" events should now be reported on a "near miss" initial report form which will be sent to the hospital on request. For the convenience of reporters events may be reported singly or in batches of up to 16 at a time. The choice will depend entirely on which system is more convenient for the reporter.

Confidentiality of data is fundamental to the success of the project.

Data are stored in a password-protected database in a secure location.

The help of the IT staff of the National Blood Service is gratefully acknowledged.

Once all the information has been gathered about an event and entered onto the database without patient, staff or hospital identifiers, all reporting forms and other paper records which contain any identifiers are shredded. The questionnaires (which have any possible identifiers removed) are kept in a secure container until data analysis for the report is complete after which they are shredded. SHOT does not provide details of individual cases, or any form of summarised data to any outside person or organisation, other than that provided in this report.

Limitations of the SHOT system

Reporting to the SHOT scheme is voluntary. We acknowledge that many incidents may go unrecognised or unreported, and that the reports analysed cannot provide a full picture of transfusion hazards.

Following consultation and after assessment of responses to the first report, the questionnaires were revised for use during the second reporting year. It has since become clear that continual revision of questionnaires is required and arrangements have been made to revise and adapt the forms on an annual basis. The data in this year's report are the last to be gathered using variations of the original questionnaires. In order to make data entry less prone to human error we have now installed a state of the art scanning system which will electronically capture data entered on a new style questionnaire. This system of scanning data requires a very specific type of questionnaire design which largely comprises tick boxes with some areas of free text. In order to make the forms

as simple as possible to complete the tick boxes are large and the text well spaced. This has had the effect of making the number of pages in the questionnaires considerably larger than in the older versions. Since this is a new venture for SHOT we would very much welcome feedback from users on the general layout and ease (or otherwise) of use.
Case assessment. Each case is assessed to ensure that it meets the case definition at the top of each chapter. Some reported cases which do not meet these definitions or which are in some other respect not strictly within our remit may be included for educational purposes, but this is made clear in each chapter. The questionnaires seek a full picture of each reported transfusion hazard, and a critical appraisal is undertaken by the SHOT co-ordinators with respect to imputability i.e. to say whether the outcome is attributable to the transfusion. This year, we have asked reporters of fatal cases to assess the imputability of the transfusion to the death.

Participation Card

From the second year of reporting onwards we have tried to ascertain the percentage of hospitals contributing to the SHOT reporting scheme. A participation card (formerly called the 'Nil to Report' card) and covering letter is sent to the chief BMS at each of the hospitals held on the SHOT mailing list. The number of hospitals eligible to participate varies each year as hospitals close, new ones are built, and Trusts merge; the number this year was 405. The participation card exercise is repeated annually with minor changes (sometimes including short surveys) to prompt hospitals to continue to report adverse events. This year the card asked 6 questions about participation and 1 question in the form of a survey. The results are detailed in chapter 5 "Overview of Results". Formerly cards were sent to the named consultant haematologist but following requests from several hospitals it was decided that laboratory staff might be better able to complete and return the card. On returning the participation card to the SHOT office, and once any queries have been resolved with the reporting hospital, a SHOT receipt is sent which can be used to provide evidence to the Clinical Negligence Scheme for Trusts (CNST) should this be required.

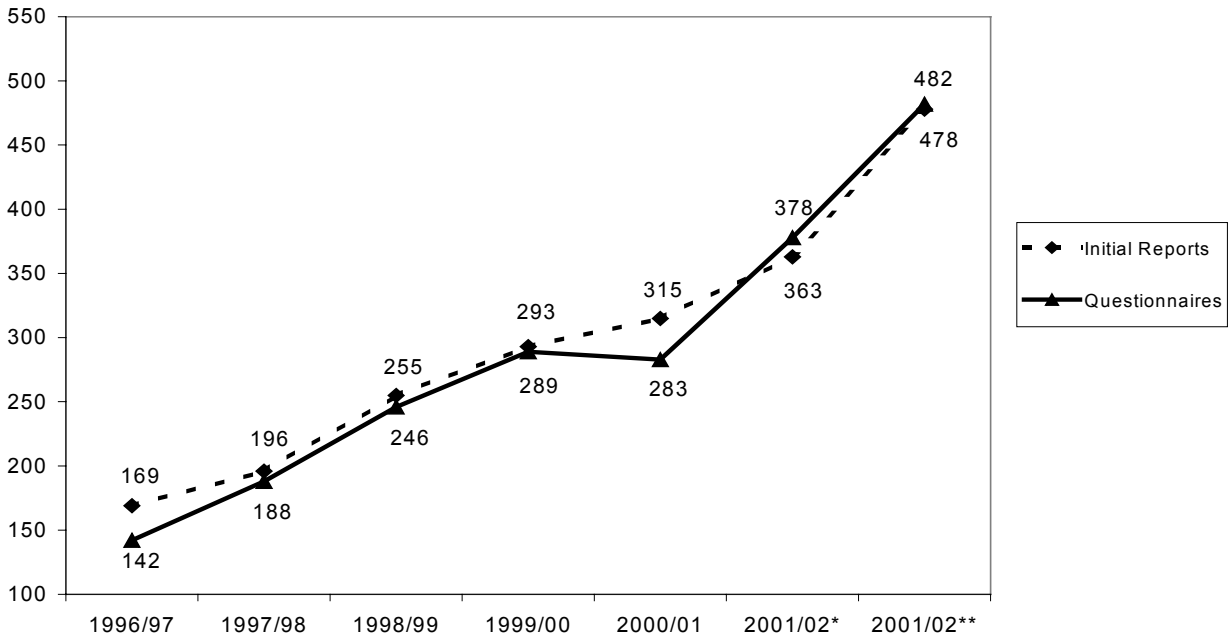
Dissemination of results

Two thousand full reports are printed annually and distributed, free of charge, to hospital haematologists and biomedical scientists in charge of hospital blood banks, chairs of professional bodies and others involved in the practice of blood transfusion. In addition executive summaries are sent to Trust Chief Executives. Last year we produced 6000 summaries but this number is felt to be too high and will be reduced this year to 4000. A small charge is made for full reports sent to non-NHS agencies and individuals. SHOT reports are made freely available on SHOT's website and those involved in the practice of transfusion medicine are encouraged to make use of the material for educational purposes. In addition members of the SHOT Standing Working Group and Steering Group are frequently asked to present data at a variety of educational meetings both in the UK and abroad.

Workload and staffing

Since the inception of the SHOT scheme in 1996 there has been a year-on-year increase in the number of reports. There may be any number of reasons for this such as heightened awareness of the importance of reporting, an increase in confidence in the guaranteed anonymity of the scheme, encouragement from the Department of Health[1, 2] or perhaps even an increase in the number of incidents occurring although this last reason is purely speculative and is unlikely, in itself, to account for a total increase of 115% in 5 years. This information is shown graphically is figure 1.

Figure 1
Increases in reporting year by year:



* 2001/02 = reports and questionnaires received before 1st October 2002
** 2001/02 = reports and questionnaires received after 30th September 2002

Although it appears from the graph that we are now receiving more questionnaires than reports, this is accounted for by the fact that we include questionnaires brought forward from the previous year which had been outstanding at the end of the reporting period.

Initial Reports

In the second to fifth years there were increases in receipt of initial reports of 167%, 30%, 15%, and 8% respectively. This year there was a further increase of 20% measured over 12 months.

Questionnaires

The numbers of reports which are eventually analysed as valid SHOT reports (whether reported by questionnaire or by letter) have, with the exception of year 5, increased annually. The apparent drop in numbers of questionnaires received in year 5 obliged us to introduce a more rigid system of follow up. The system has worked well and this year has seen receipt of questionnaires increase again. The percentage increases or decreases since reporting began are 33%, 31%, 17%, -2%, and 34%.

SHOT Personnel

The introduction of a new IT system together with the ongoing increase in numbers of reports and the intention to undertake additional projects has led to a need for a review of staffing levels and skill mix. At the time of going to press there are 3 full time paid employees in addition to the National Medical Co-ordinator who is now paid for 6 sessions per week. The 3 office posts are described here.

1. The assistant national co-ordinator (ANC) whose duties include managerial responsibility for the other staff, the development and enhancement of office procedures and systems including the database, attendance at meetings, conferences etc. and the co-ordination of report writing.

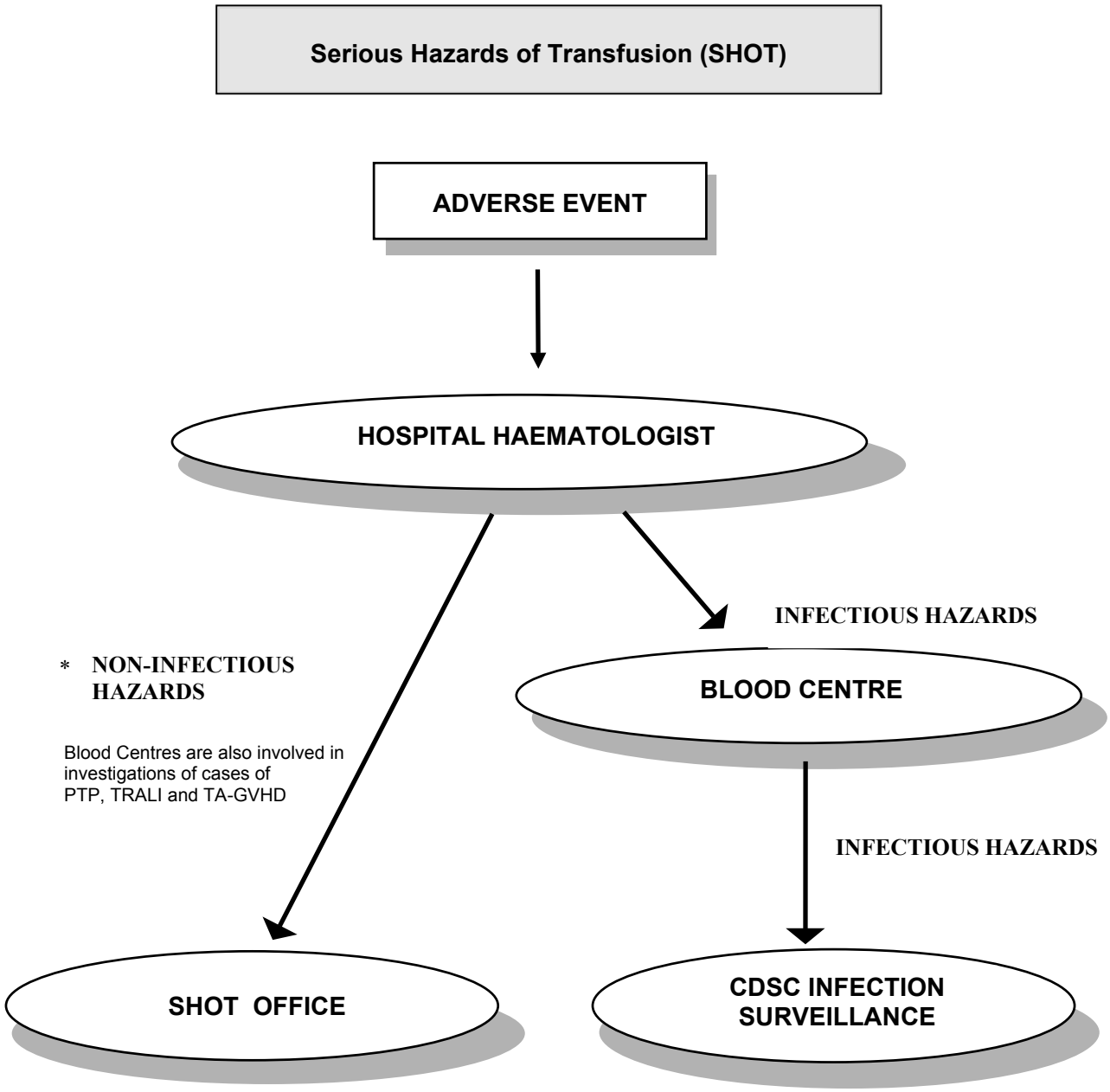
2. The data collection and management officer. This post was developed with the intention of taking on full responsibility for the maintenance and further development of the databases as well as the SHOT website. This staff member is also expected to deputise for the ANC.

3. The Personal Assistant to the ANC, whose role has developed and expanded considerably since the beginning of the scheme. This member of staff handles all the bulk work associated with the clerical processes involved in data collection as well as providing a good secretarial service, meetings and conference organisation, and dealing with telephone enquiries.

The SHOT office welcomes comments and suggestions on ways to improve the service it provides. With more than 400 hospitals eligible to participate in SHOT, maintenance of an accurate mailing list is extremely difficult and we rely on the good will of hospital staff to keep us informed by notifying the office of changes in personnel responsible for SHOT reporting.

Apart from the National Medical Co-ordinator, the Assistant National Co-ordinator and the National Co-ordinator for infectious hazard reporting (who has a joint paid appointment with the NBS and the Health Protection Agency) members of the SHOT Standing Working Group and Steering Group give their time free of charge to SHOT by arrangement with their respective employing authorities.

Figure 2
SHOT reporting system flow chart



* Incorrect blood/component transfused
* Major acute or delayed reaction
* Transfusion-related graft-versus-host disease
* Transfusion related acute lung injury
* Post- transfusion purpura
* Autologous pre-deposit : donor incident
* Near miss events

5. OVERVIEW OF RESULTS 2001-2002

The data in this report are derived solely from the initial report forms, and from subsequent analysis of questionnaires and explanatory letters. All questionnaires were examined by the co-ordinators to identify inconsistencies in the information provided and, where these occurred, the reporting clinician was contacted for clarification of the event.

Historically the year end date for SHOT reporting has been 30th September. This reflected the fact that the scheme was launched officially on 18th November, 1996 but included incidents which occurred between 1st October 1996 and 30th September 1997. Following publication of the first report the system of analysis was changed to examine incidents by date of initial report rather than date of incident. This enabled us to carry forward incidents occurring at the end of the reporting year and for which the completed questionnaire did not arrive before the closing date. This system, in place since year 2, continues today but this year we have taken steps to bring the scheme in line with other major confidential enquiries by changing the year end to 31st December. This change in year end has two main consequences. Firstly it means that publication of the annual report will now move to July from April. Secondly for this year only we are presenting data collected over a 15 month period from 1st October 2001 to 31st December 2002. In subsequent years we will revert back to a 12 month period covering 1st January to 31st December. Where comparisons are desirable this year with statistics from the last report the figures will either be quoted separately or will be adjusted for the unequal time periods.

Overview of reports and participation cards

Number of hospitals

Of the 405 hospitals eligible to participate in the scheme this year, 187 (46%) submitted initial reports during the 15 month reporting period. Results obtained from the annual participation card showed that a further 191 hospitals stated that they had not seen any incidents. Combining these two figures gives an overall participation rate of 93% (378 participating hospitals).

2001-2002 Participation Survey

Hospitals were asked 4 questions about their participation, 2 about the number of incidents they had seen and 1 question designed to elicit information about hospital policy with regard to the numbers of staff performing the bedside check. Cards were sent to 405 hospitals and 373 (92%) returned them. Table 1 shows the results from questions about participation.

Table 1
Participation Survey 2001-2002 Results

	Yes	No
Question 1 371 responses (99.2%) Did your hospital experience any SHOT incidents in the period 1st October, 2001 to 31st December, 2002?	180 (48.5%)	191 (51.5%)
Question 3 178 responses (99%) Did you report all of them to the SHOT office?	174 (98%)	4 * (2%)
Question 4 * 368 responses (98.6%) Did your hospital experience any "near miss" incidents in the period 1st October, 2001 to 31st December, 2002?	204 (55.4%)	164 (44.6%
Question 6 * 204 responses (100%) Did you report all of them to the SHOT office?	147 (72%)	57 (28%)

* See further notes below

Notes

1. Although 4 hospitals said that they had not reported all their SHOT incidents, the question was phrased in such a way that we do not know whether they reported some incidents or none.

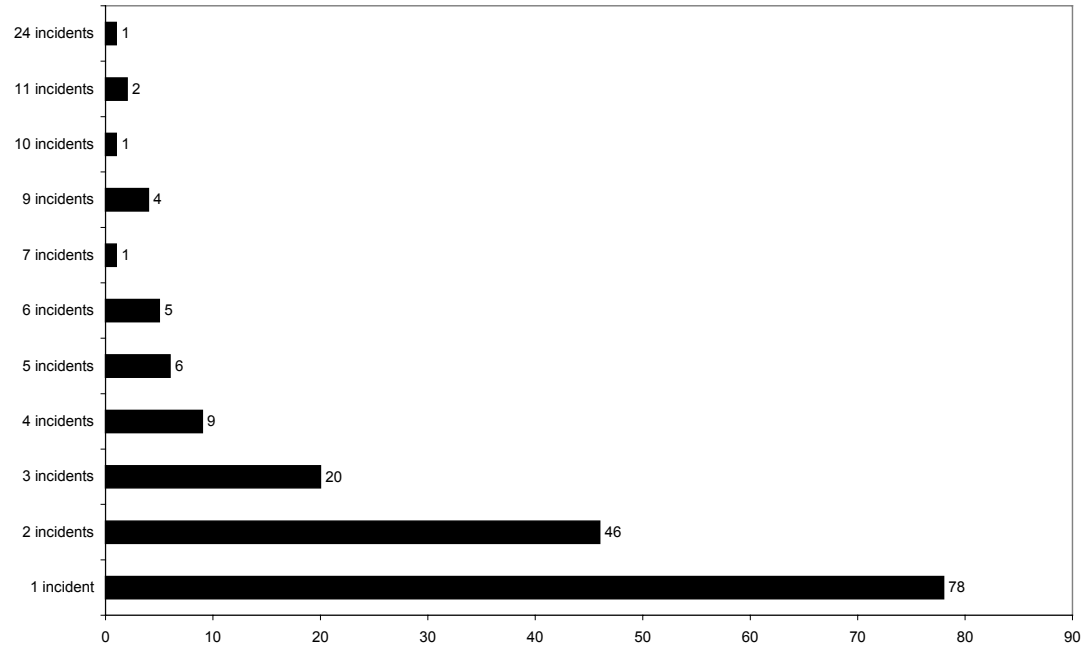
2. Whereas 97% of hospitals said that they had reported all their incidents to SHOT, in the case of "near miss" events 28% said that they had not reported all of them. This may reflect the fact that "near miss" events are more numerous than full incidents and hospitals therefore have less time to report them.

3. The following comments were received from reporters in response to the "near miss" events questions:

- Aware of under reporting (2)
- None reported to SHOT (1)
- Not all reported (1)
- Not currently reporting but will try to do so (1)
- Currently reporting to internal incident reporting system only (1)

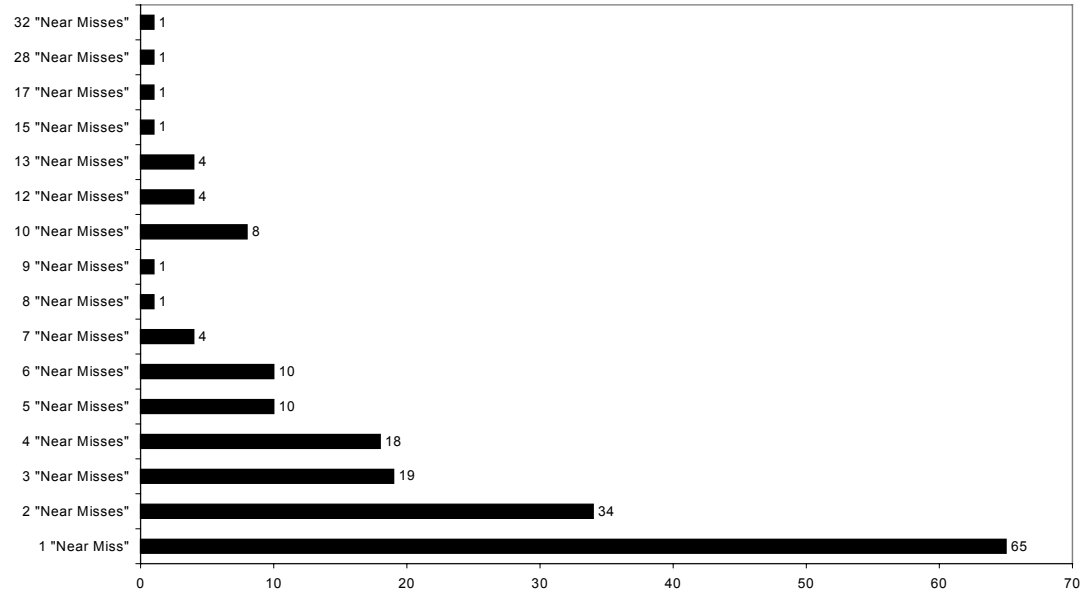
In response to the question "How many incidents did your hospital see?" 173 respondents replied giving a total between them of 425 incidents. This gives an average figure of 2.5 incidents per hospital. However the numbers of incidents reported by individual hospitals varies greatly. Figure 3 shows these data graphically.

Figure 3
Numbers of incidents reported by individual hospitals



Numbers of "near miss" events seen by individual hospitals are, understandably, higher. A total of 689 incidents were seen by 182 hospitals giving an average of 3.8 incidents. However some reporters were unable to say how many incidents they had seen commenting that there had been too many to count. Clearly this distorts the results but the figures which were given are shown graphically in figure 4.

Figure 4
Numbers of "near miss" events reported by individual hospitals



The results of the survey on local policy for bedside checking are interesting. A BCSH guideline[6] recommends that one member of staff should be responsible for this vital final check. However the result of this survey suggests that the recommendation is not being followed by a majority of hospitals. Of the 373 hospitals who returned cards all but 3 responded to this question giving an overall response rate of 99.2%. One person checking is practiced in 67 hospitals but 2 person checking continues to be the norm in 303 hospitals (81%).
Eighteen respondents made additional comments on this question. Their comments are shown in table 2.

Table 2
Additional comments on 1 versus 2 person checking

Hospitals who said 1 person was responsible for bedside checking
• Policy states 1 but most nurses still check in pairs • At least one trained member of staff (medical or nursing) • Must be registered nurse, midwife, or doctor holding IV certificate • Although only 1 area doing 1 nurse checking, most stay with 2 • 1 person recommended but 2 given as an alternative
Hospitals who said 2 people were responsible for bedside checking
• One person checking is being piloted on some wards • Checked independently • Plans to change to 1 person checking • Currently being discussed with a view to changing to 1 person • Bedside check independently at separate times before transfusion • As drug administration with the Trust requires 2 signatures & for consistency this was kept the case for transfusions • If situation dictates, can be done by 1 qualified person • I believe 1 person checking is better • I believe our hospital policy has it right with 2 people needed to do the bedside check • But we feel that 1 person doing it properly would be safer • Considering reviewing ourselves • 1st checker has full responsibility, 2nd checker confirms • Piloting unit tracking system which tracks unit from issue and includes check verifications as well

Number of reports

In the 15 month period from 1st October 2001 to 31st December 2002 a total of 478 initial reports were received of which 363 were received before 1st October 2002. The 363 received in this initial 12 months represents an increase of 15.2% over the 315 received in the preceding 12 month period. Using the same time period for comparison the largest category is, once again, "incorrect blood component transfused" this year showing an increase of 21% (258 reports) over the 213 received last year. The numbers of reports in each category received since SHOT reporting began is shown in table 3.

Table 3
Adverse events reported during the five reporting years 1996/97 to 2001/02

	1996/1997	1997/1998	1998/1999	1999/2000	2000/2001	2001/2002 *
IBCT	81	110	144	201	213	258(343)
ATR	27	28	34	34	37	38(49)
DTR	27	24	31	28	40	33(46)
PTP	11	11	10	5	3	3(3)
TA-GVHD	4	4	4	0	1	0(0)
TRALI	11	16	16	19	15	26(32)
TTI	8	3	9	6	6	5(5)
Unclassified	0	0	7	0	0	0
TOTAL	**169**	**196**	**255**	**293**	**315**	**363(478)**

IBCT: Incorrect blood component transfused
ATR: Acute transfusion reaction
DTR: Delayed transfusion reaction
PTP: Post-transfusion purpura
TA-GVHD: Transfusion associated graft-versus-host-disease
TRALI: Transfusion-related acute lung injury
TTI: Transfusion transmitted infection

***** The figures in brackets are the total numbers of reports received during the full 15 month period 1st October, 2001 to 31st December, 2002.

Figure 5
Comparison of initial reports of incidents since reporting began in 1996

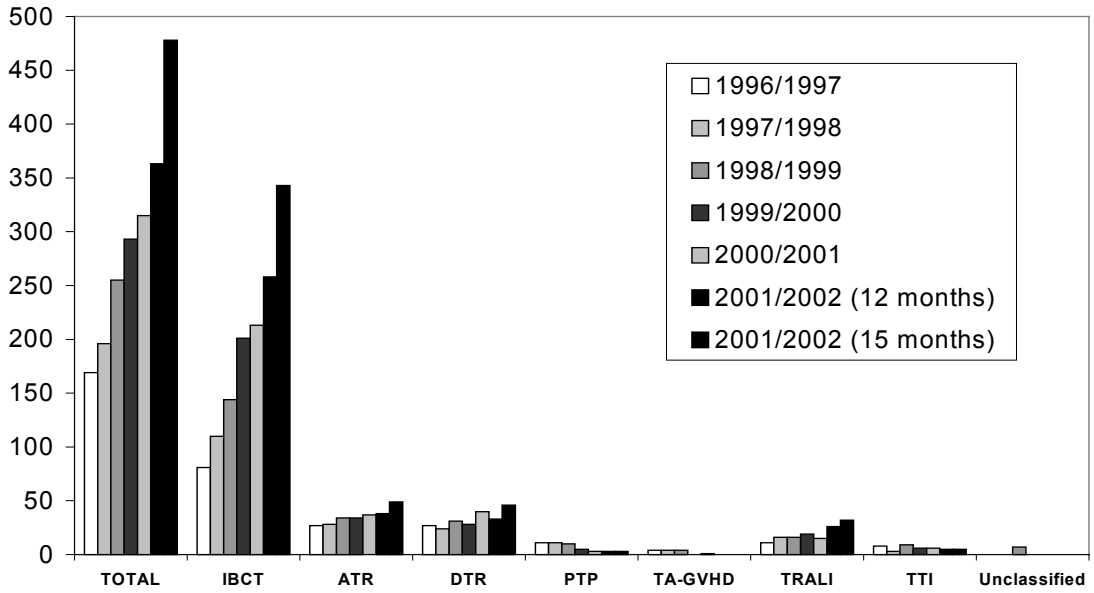
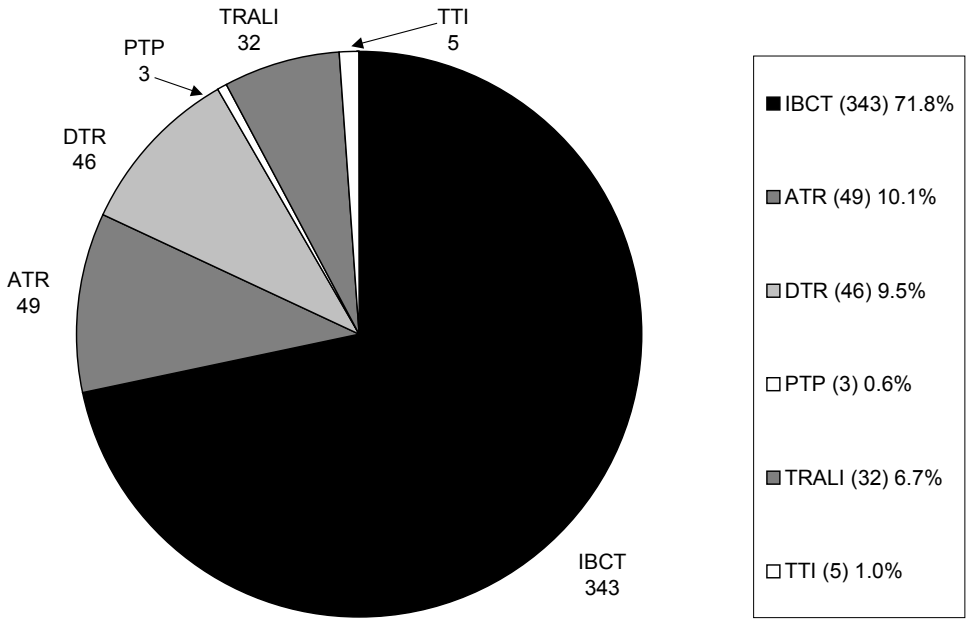


Figure 6
Overview of 478 cases for which initial reports forms were received over 15 months.



In addition to the 478 initial report forms shown above a further 27 were received which were withdrawn because they were not considered to be valid SHOT reports and 12 were written off when it became clear, despite extensive following up by SHOT office staff, that the questionnaires would not be returned. Details of the withdrawn cases are summarised in table 4.

Table 4
Initial report forms withdrawn from the analysis

- **10 were withdrawn by the reporter**
- **16 were withdrawn by the SHOT analyst**
- **1 was withdrawn by the National Medical Co-ordinator**

The 10 withdrawn by the reporter

IBCT (7)	1 x Unavoidable non-detection of anti-E. 1 x No reaction observed in the patient * 1 x Unavoidable issue of incompatible units in an emergency. 3 x No product transfused. 1 x Clinical decision to use incompatible, non-irradiated unit in an emergency.
ATR (1)	1 x Reaction not due to transfusion.
DTR (2)	1 x Reaction no longer thought to be due to transfusion. 1 x No reaction noted by ward staff.

* This case should, in fact, have been reported to SHOT. The fact that an incorrect or inappropriate unit given does not produce any reaction in a patient should not deter hospitals from reporting. On this occasion, however, the reporter could not be persuaded by SHOT office staff to complete a questionnaire.

Table 4 continued

The 16 withdrawn by the SHOT analyst

IBCT (7) 2 x Clinical decision to transfuse an incompatible unit in an emergency.
1 x Laboratory decision to over-ride computer warning.
1 x Failure of protocol but the blood would have been transfused anyway.
1 x Breach of local protocol but not of national guidelines.
1 x Failure to give anti-D = drug administration error
1 x Anti-D given instead of Hep B Ig = drug administration error.

ATR (4) 3 x Febrile reaction only.
1 x Suspected "white coat" syndrome.

DTR (1) 1 x No evidence of delayed transfusion reaction.

PTP (1) 1 x Serology negative and platelet count low before transfusion.

TRALI (3) 3 x Not thought to be TRALI

The 1 withdrawn by the National Medical Co-ordinator

IBT (1) 1 Patient received stock intravenous immunoglobulin (IVIgG) instead of trial IVIgG

Analysis of questionnaires

Excludes 5 TTI cases

A total of 477 incidents (including 2 IBCT reported by letter rather than questionnaire) were analysed for this report. Thirty-eight of these were outstanding from the previous year. A further 39 initial report forms were received during the reporting period for which no questionnaires were received by the closing date. These will be analysed next year. In last year's report we identified 46 initial report forms for which no questionnaires were received. We have been unable to obtain sufficient information to allow analysis on 4 cases outstanding from last year and these cases will not be pursued further. Additionally 4 were eventually withdrawn by the originating reporter.

Table 5
Summary of completed questionnaires received.

	IBCT	ATR	DTR	PTP	TA-GVHD	TRALI	TTI	Totals
Total number of reports received	343	49	46	3	0	32	5	**478**
Questionnaires included in analysis	346(27)	48(5)	47(3)	3	0	33(3)	5	**482**
Questionnaires outstanding	25	6	2	0	0	6	0	**39**

These figures include questionnaires outstanding from last year shown in brackets

Figure 7
Overview of 482 cases for which fully completed questionnaires were received

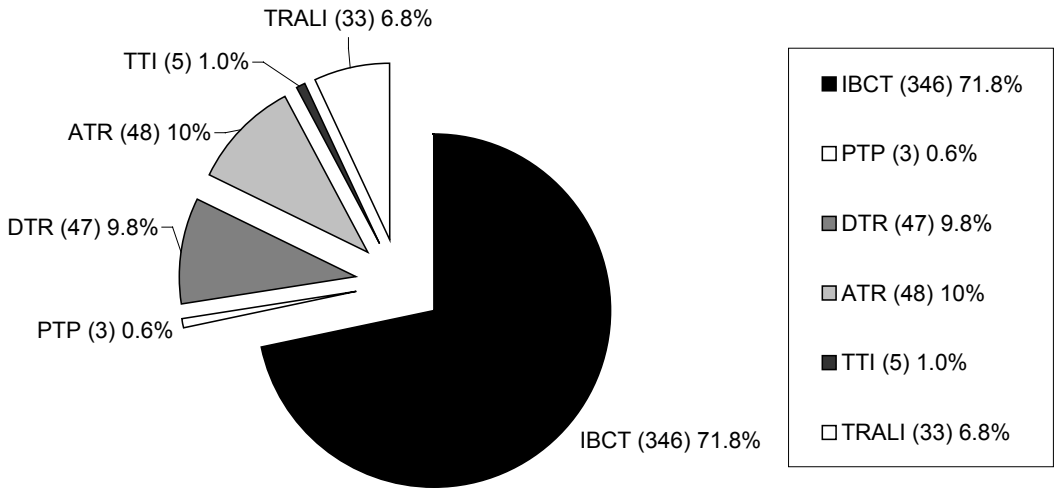


Figure 8
Overview of transfusion related mortality/morbidity data reported in 482 completed questionnaires.

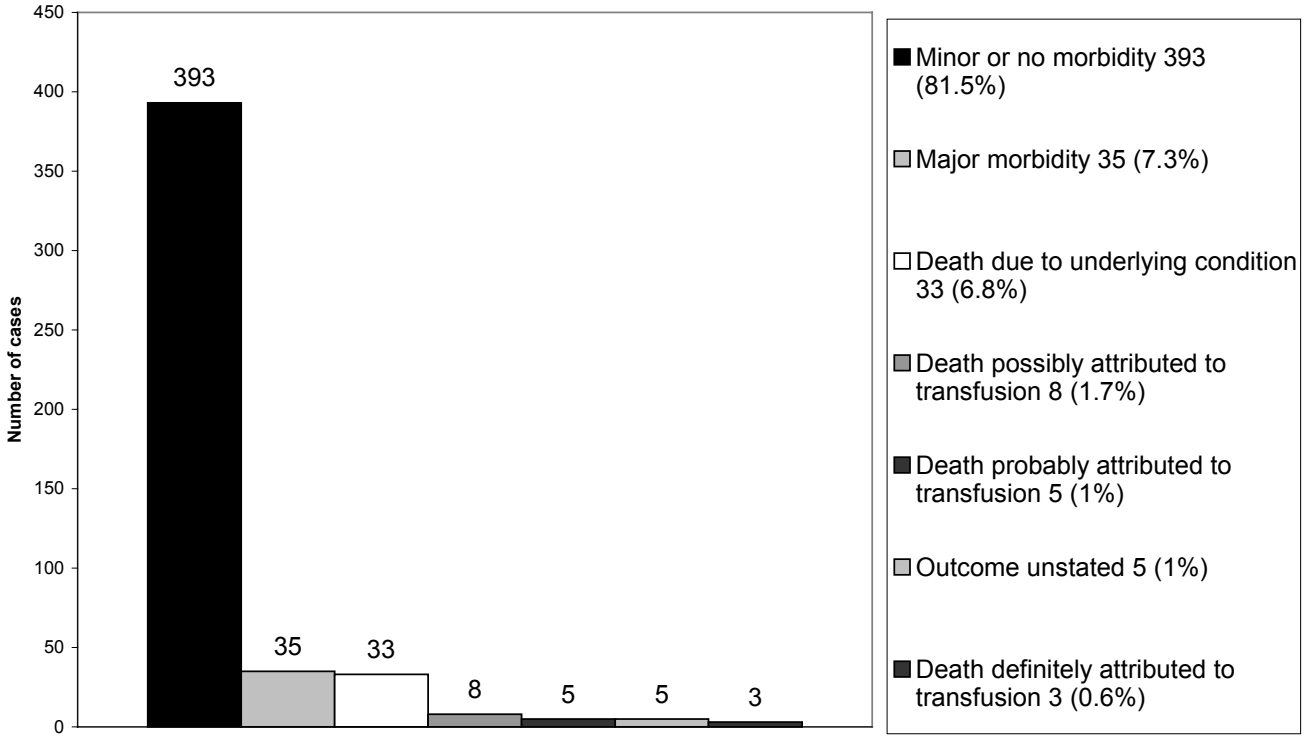


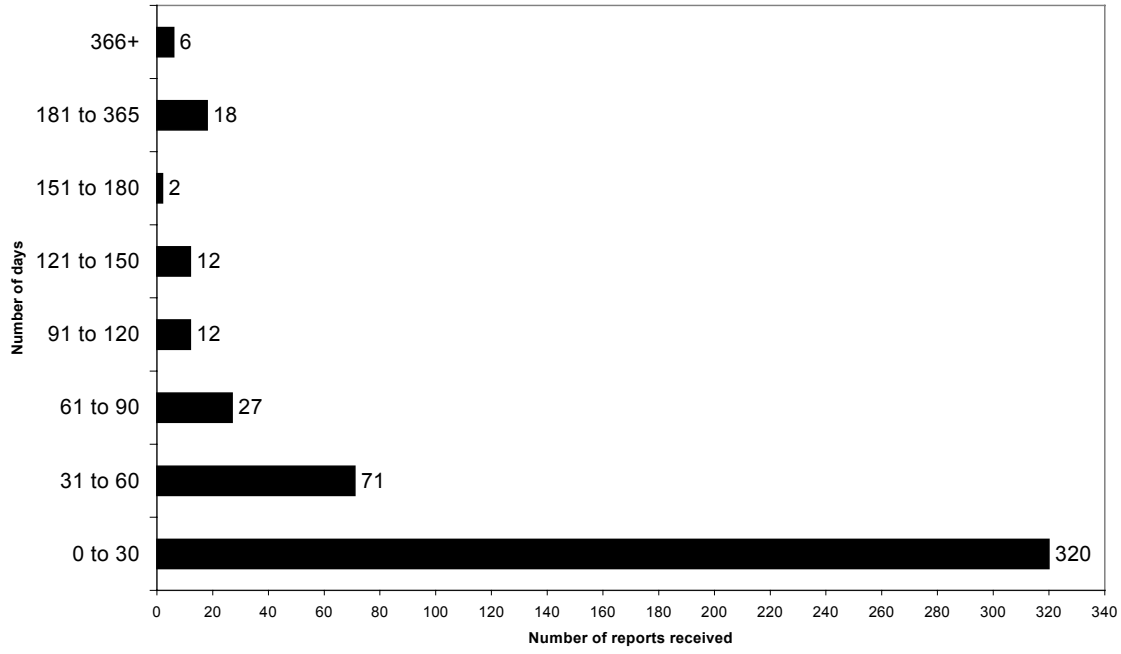
Table 6
Transfusion related mortality/morbidity according to the type of hazard reported in 482 completed questionnaires.

	Total	IBCT	ATR	DTR	PTP	TRALI	TTI
Death definitely attributed to transfusion	**3**	0	0	2	0	1	0
Death probably attributed to transfusion	**5**	1	1	1	0	2	0
Death possibly attributed to transfusion	**8**	3	1	0	0	4	0
Death due to underlying condition	**33**	18	5	6	0	4	0
Major morbidity	**35**	9	0	2	1	18	5
Minor or no morbidity	**393**	310	41	36	2	4	0
Outcome unstated	**5**	5	0	0	0	0	0
Totals	**482**	**346**	**48**	**47**	**3**	**33**	**5**

Major morbidity was defined as the presence of one or more of the following:

- ◊ Intensive care admission and/or ventilation
- ◊ Dialysis and/or renal dysfunction
- ◊ Major haemorrhage from transfusion-induced coagulopathy
- ◊ Intravascular haemolysis
- ◊ Potential RhD sensitisation in a female of child-bearing potential
- ◊ Persistent viral infection
- ◊ Acute symptomatic confirmed infection (viral, bacterial or protozoal)

Figure 9
Calendar days between transfusion incident and initial report to SHOT (n=468) *



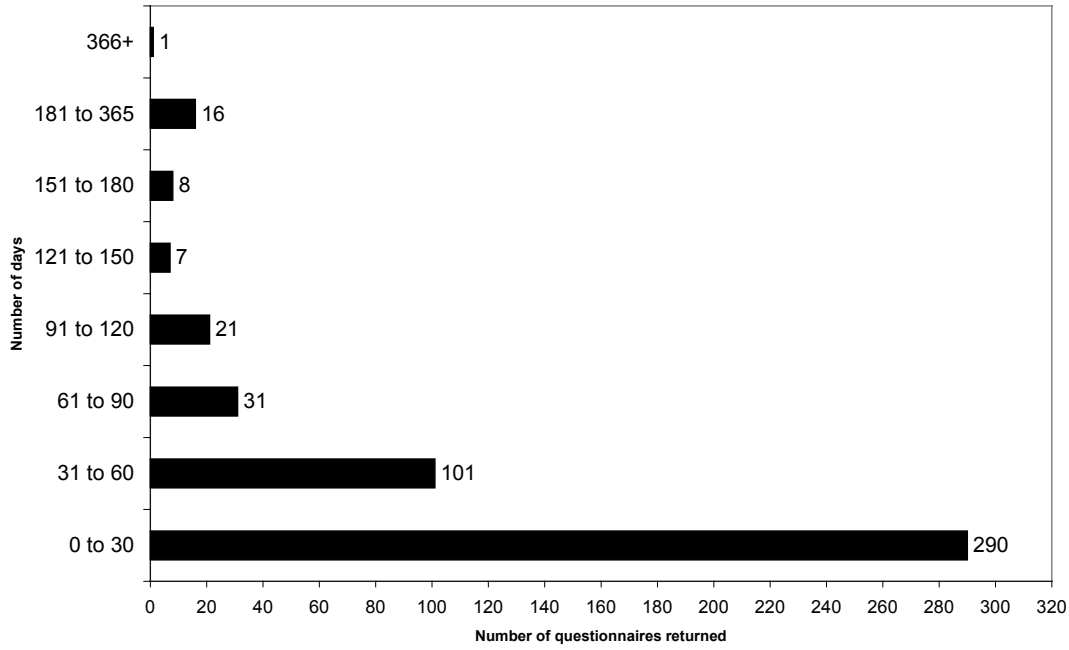
* Excludes 5 TTI and 9 where the date of transfusion was not stated or not known

The median time for return of initial reports was 17 days. This time interval has been stable since year 2. The figures for reporting years 2, 3, 4 and 5 were 15, 17, 15 and 16 days respectively compared with 30 days for the first reporting year. There were 6 cases which had very lengthy delays between the incident and reporting it. The reasons the reporters gave for this were:

- Originally reported as an ATR. At that time the time interval was only 10 days. However on review the SHOT analyst considered that this should be reported as in incorrect component transfused. By the time the incident was reported the second time the interval was 1 year.
- Originally reported as a "near miss" incident with a time interval of 13 days. Analysts requested that the case be re-reported as an IBCT by which time the interval was 1 year 2 months.
- Another case reported originally as a "near miss" which ought to have been reported as an IBCT However the original time interval between incident and reporting the "near miss" was still very lengthy at 2 years 3 months. The reporter gave no explanation and the re-classification of the case to IBCT increased the time interval to 3 years 2 months
- Anti-D was given in error to a RhD positive woman. The error was not discovered until she was grouped again for a subsequent pregnancy almost 2 years later.
- A group O RhD positive woman was transfused with group B RhD positive red cells. This error was not recognised until the patient was readmitted 1 year 10 months later.
- A TRALI case with an interval between transfusion and reporting of 1 year. The reporter did not give an explanation.

Figure 10
Calendar days between initial report and return of completed questionnaire (n =475)

Excludes 5 TTI, and 2 IBCT reported by letter



The median time between initial report and return of final questionnaire was 21 days. This is an improvement for the second year running. Last year's median time was 26 days and the previous year 33 days.

Overall transfusion activity and patient characteristics

The number of incidents reported needs to be placed in the context of the overall numbers of transfusions taking place. Table 7 gives details of total blood component issues from the four UK Transfusion Services (England, Scotland, Wales and Northern Ireland). This information represents components issued during the fiscal year 1st April, 2001 to 31st March, 2002

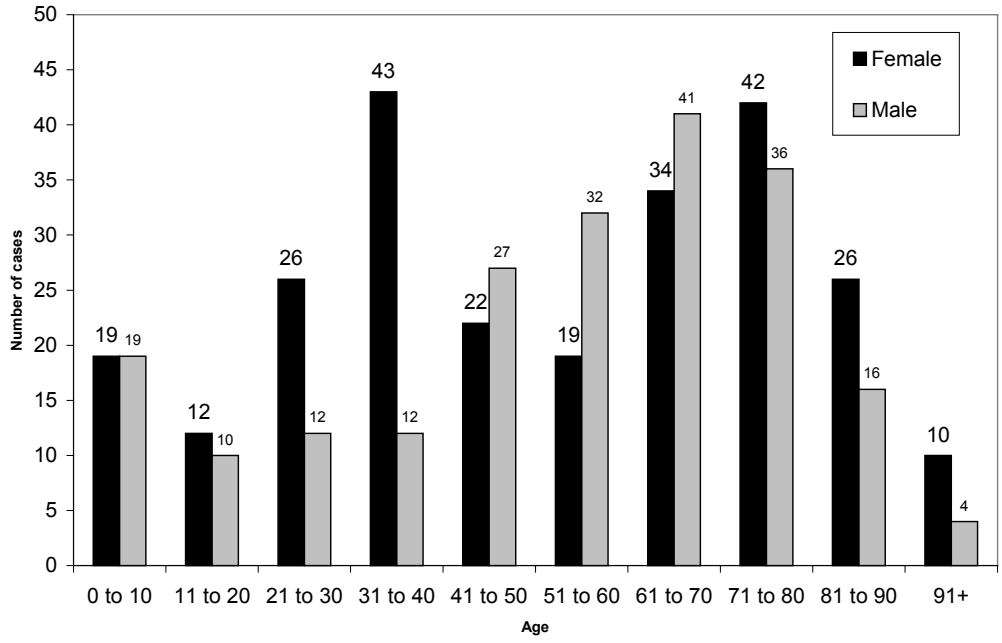
Table 7
Total issues of blood components from the Transfusion Services of the UK in 2001/2002

Red Cells	**2,683,463**
Platelets	**251,451**
Fresh frozen plasma	**385,236**
Cryoprecipitate	**88,253**
TOTAL	**3,408,402**

In previous years, data from the participation cards have been used to determine what percentage of all red cells issued were being received and handled by what percentage of participating hospitals. This question was interpreted in different ways and the data obtained were inconsistent, therefore this question was omitted altogether from this year's card. We are currently exploring ways of obtaining reliable data from the Blood Services' databases whilst continuing to maintain hospital confidentiality.

Figure 11
Distribution of patients by age and gender at the time of transfusion (n=462)

Excludes 5 TTI and 15 cases where either gender or age was not stated or not known



	Females (253)	**Males (209)**
Age range	less than 1 day to 98 years	less than 1 day to 94 years
Median Age	53 years	59 years

6. CUMULATIVE DATA 1996 - 2002

In this sixth year of SHOT reporting we continue to build on earlier data to provide an increasingly authoritative analysis of serious transfusion complications in the UK. In particular accumulated data on overall mortality/morbidity figures will illustrate outcomes over several years and should inform policy decisions on allocation of resources to blood safety initiatives. This chapter also presents in cumulative form extracts from the full chapters on Incorrect Blood Component Transfused, Acute Transfusion Reaction, Delayed Transfusion Reactions and Near Miss Events.

Initial report forms received:	**1711**	**Questionnaires analysed:**	**1630**

Figure 12
Initial reports by incident 1996/97 - 2001/02 (n=1711)

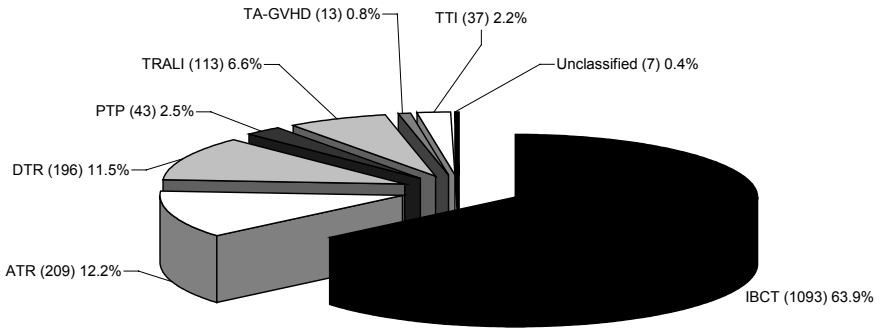


Figure 13
Questionnaires by incident 1996/97 - 2001/02 (n= 1630)

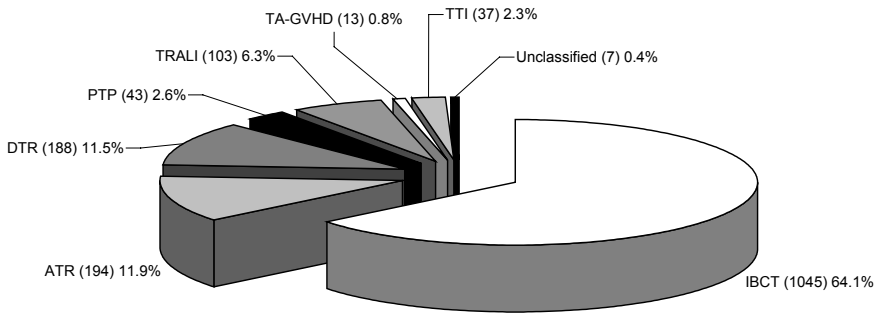


Figure 14
Overall mortality/morbidity figures 1996/97 - 2001/02 (n=1630)

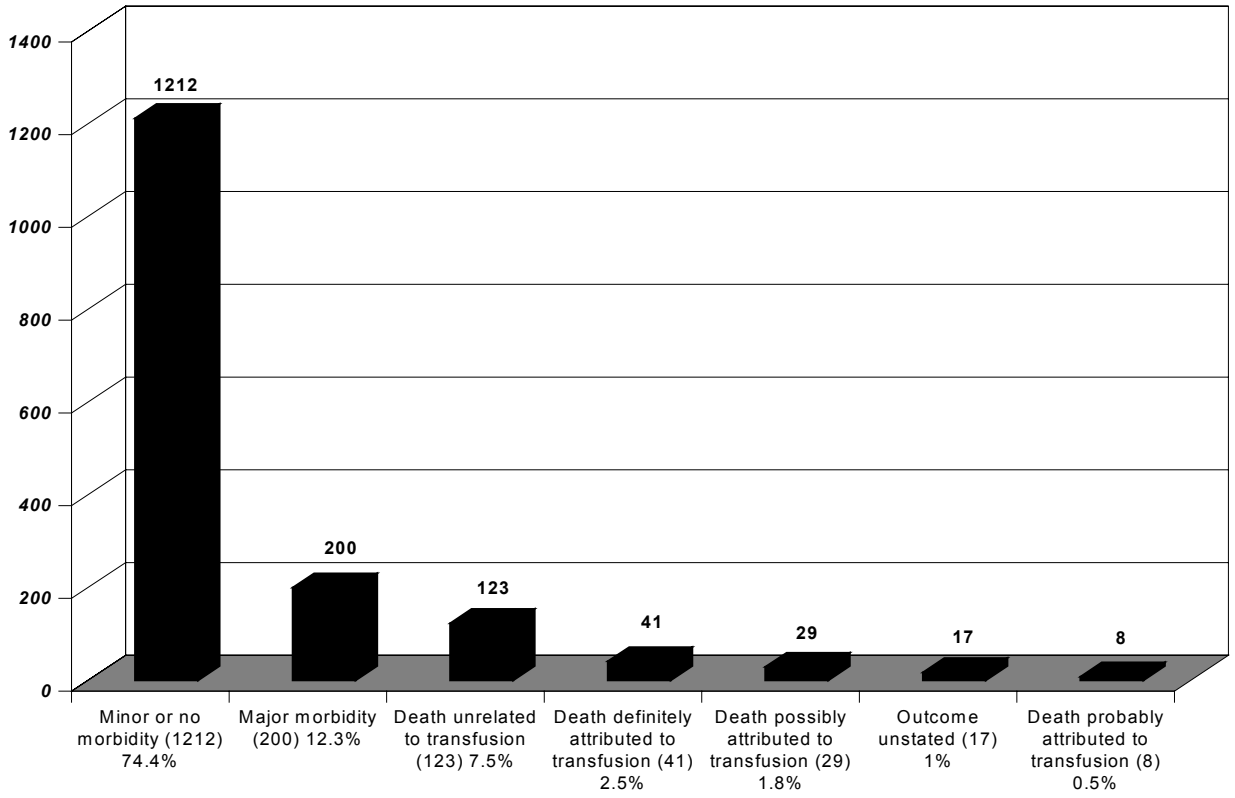


Table 8
Overall mortality/morbidity figures by fully analysed questionnaires 1996/97 – 2001/02 (n=1630)

	Total	IBCT	ATR	DTR	PTP	TA-GVHD	TRALI	TTI	UC[1]
Minor or no morbidity	1212	876	162	139	26	0	4	0	5
Major morbidity	200	69	3	20	12	0	67	29	0
Death definitely attributed to transfusion	41	5	2	6	1	13	7	7	0
Death probably attributed to transfusion [2]	8	2	1	1	0	0	4	0	0
Death possibly attributed to transfusion [3]	29	8	5	1	1	0	14	0	0
Death unrelated to transfusion	123	74	18	20	3	0	7	1	0
Outcome unknown	17	11	3	1	0	0	0	0	2
Totals	**1630**	**1045**	**194**	**188**	**43**	**13**	**103**	**37**	**7**

[1] UC = unclassified incidents from 1998/99 report
[2] This category included for the first time from 1999/2000
[3] This category included for the first time from 1998/1999

Incorrect Blood Component Transfused cases 1996/97 - 2001/02

Initial report forms received:	**1093**	**Questionnaires analysed:**	**1045**

Table 9
Mortality/morbidity data for IBCT cases (n=1045)

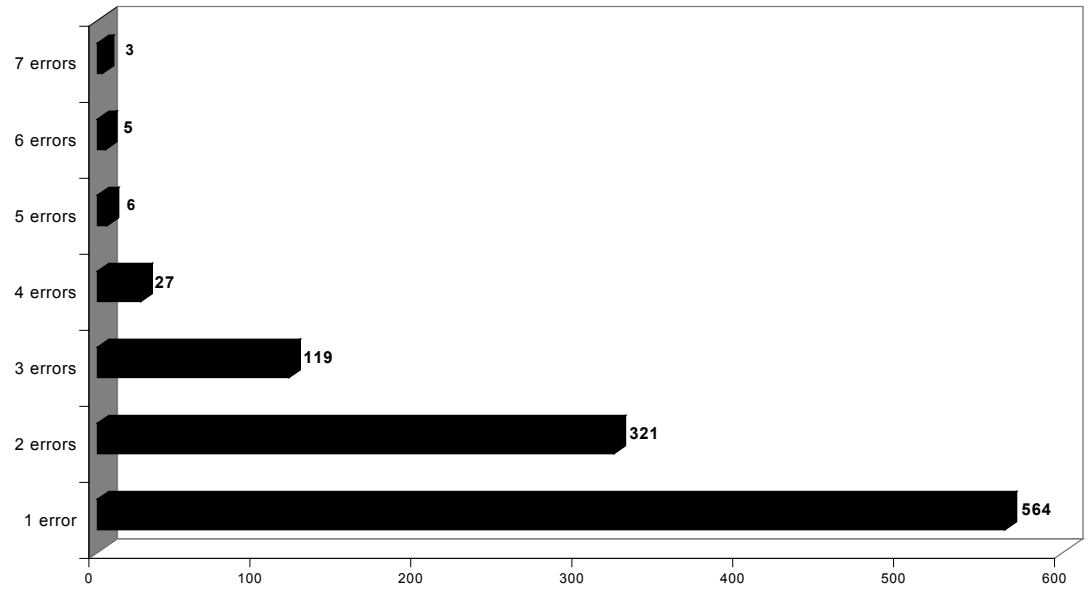
OUTCOME	NUMBER OF CASES
Death definitely attributed to transfusion	5
Death probably attributed to transfusion *	2
Death possibly attributed to transfusion	8
Death unrelated to transfusion	74
Major morbidity	69
Minor or no morbidity	876
Unknown outcome	11
Total	**1045**

***** This category introduced 1999/2000

Table 10
Outcome of cases of IBCT 1996/97 – 2001/02 (n=1045)

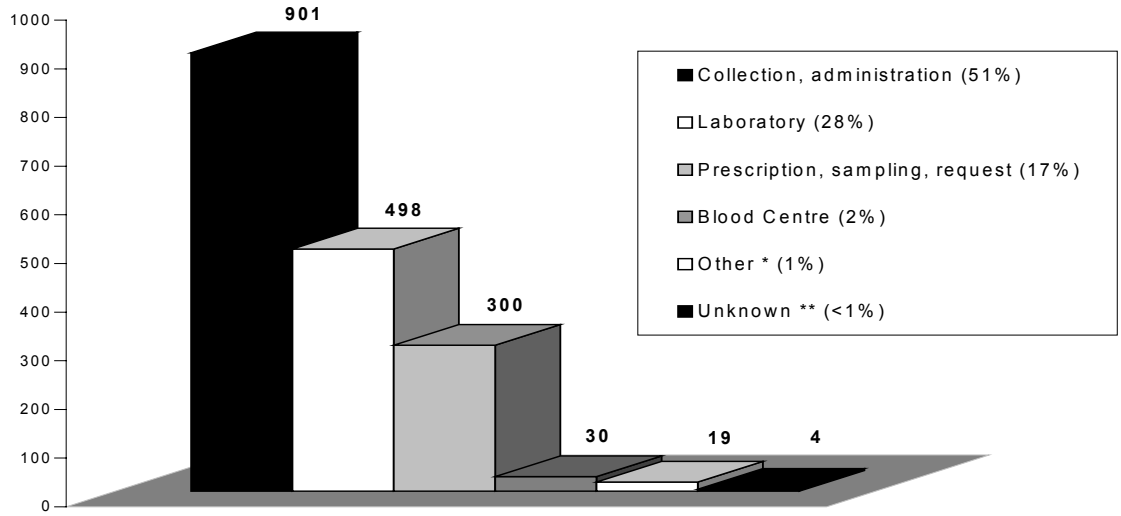
Category	Survived/ no ill effects	Major morbidity	Died unrelated to tx.	Died possibly related to tx.	Died probably related to tx.	Died definitely related to tx.	Unknown	TOTAL
Major ABO incompatibility	125	41	15	5	1	5	1	**193**
RhD incompatible	69	18	5	0	0	0	0	**92**
ABO/RhD compatible	281	0	16	1	0	0	3	**301**
Other red cell incompatibility	44	5	5	0	0	0	1	**55**
Inappropriate transfusion	79	2	7	2	1	0	1	**92**
Special requirements not met	182	2	17	0	0	0	4	**205**
Anti-D	80	0	0	0	0	0	0	**80**
Other	15	0	0	0	0	0	0	**15**
Blood group not stated	1	1	9				1	**12**
Total	**876**	**69**	**74**	**8**	**2**	**5**	**11**	**1045**

Figure 15
Multiple errors in IBCT cases 1996/97 - 2001/02 (no cases=1045, no. errors=1752)



The average number of errors per case over 6 years is 1.7 and has been consistent each year with averages of 2.3 in year 1, 1.4 in year 2, 1.8 in year 3, and 1.7 in years 4, 5 and 6.

Figure 16
Distribution of errors in IBCT cases 1996/97 - 2001/02 (no. cases=1045, no. errors=1752)



* **Other** = Year 4: 2 errors involved transport between hospitals and 4 errors could not be traced to their source. Year 5: 2 cases of expired albumin where it was not possible to determine who was responsible for maintaining stocks, 2 cases of a communication failure between the hospital transfusion laboratory and the ward, 1 case of a patient who had duplicate hospital records but with completely different dates of birth, and 1 case where it is thought that the patient's Hb result was written wrongly in the notes. Year 6: 4 incorrect Hb results, unable to determine cause and 3 failures of hospital blood bank refrigerators.

** **Unknown** = Year 5: 4 cases where it was not possible to determine the source of the error.

Table 11
Laboratory errors and grade of staff involved 1996/97 - 2001/02
(488 errors in the 411 cases where this information was available)

Error	Total number of errors	State registered BMS, routine, regularly working in blood bank	State registered BMS, on call, regularly in blood bank	State registered BMS, on call, not regularly in blood bank	Other staff	Unstated
Sample transposition	**17**	7	6	4	0	0
Failure to consult/heed historical record	**61**	31	9	16	2	3
Incorrect group	**110**	48	23	29	1	9
Missed antibody screen	**21**	8	3	7	0	3
Missed incompatibility/ crossmatch error	**26**	7	9	8	0	2
Incorrect labelling of component	**34**	25	3	4	1	1
Selection/issue of inappropriate component	**81**	38	12	19	5	7
Failure to clear satellite refrigerator	**16**	15	0	0	0	1
Failure to irradiate	**20**	12	3	2	1	2
Clerical error	**26**	13	5	2	1	5
Other procedural error	**60**	25	7	18	0	10
Other	**14**	9	2	0	0	3
Unknown	**2**	1	0	1	0	0
Total	**488**	**239**	**82**	**110**	**11**	**46**

Immune complications 1996/97 - 2001/02

Acute Transfusion Reactions

Initial report forms received:	**209**	**Questionnaires analysed:**	**194**

Table 12
Acute reaction types 1996/97 - 2001/02 (total cases = 194)

RED CELLS (86)		**FFP (54)**	
Haemolytic or Incompatibility*	26	Anaphylactic	25
Non-haemolytic febrile	25	Allergic	23
Hypotensive	2	IgA antibodies	1
IgA antibodies	1	Hypotension	2
Anaphylactic	10	Cardiac Failure	2
Allergic	12	Febrile	1
Dyspnoea/chest pain/rigors	4		
Other**	6		
PLATELETS (50)		**RED CELLS with FFP (combined)(1)**	
Hypotension +/- flushing	8	Hypertransfusion	1
Haemolytic	6		
Anaphylactic	19	**RED CELLS with PLATELETS (combined) (1)**	
Allergic	14		
Chest pain +/- dyspnoea	2	Allergic	1
Generalised pain + hypotension	1		
RED CELLS, CRYOPRECIPITATE, FFP, PLATELETS (combined) (1)		**FFP with PLATELETS (combined) (1)**	
Fluid overload	1	Allergic	1

* incompatibility = febrile reaction considered to be due to the presence of a red cell antibody (detected in Transfusion Laboratory)
** (↑BP x 1; jaundice x 1; haemoglobinuria x 1; hypoxia/acidosis in neonate x 2; neutropenia x 1)

Acute reactions to red cells are proportionately far less frequent than reactions to either FFP or platelets. Table 13 shows the number of units of RBC, FFP and platelets issued over 6 years against the number of acute reactions reported.

Table 13
Products issued against reactions reported

	RBC (millions)	FFP (millions)	Platelets (millions)
	15.7	2.3	1.6
Numbers of reactions reported	86	54	50
	(0.0005%)	(0.002%)	(0.003%)

Reactions to FFP are 4 times more frequent than those to RBC and reactions to platelets are 6 times more frequent**.**

Delayed Haemolytic Transfusion Reactions 1996/97 - 2001/02

Initial report forms received:	**196**	**Questionnaires analysed:**	**188**

Signs and symptoms of delayed reactions are divided into 4 categories as follows: *****

Group 1 (n=27) : Asymptomatic (± positive DAT ± spherocytes)
Group 2 (n=44) : Falling haemoglobin (↓Hb)/positive DAT/spherocytes (2 of these parameters)
Group 3 (n=96) : ↓Hb + jaundice ± positive DAT ± spherocytes
Group 4 (n=19) : As group 3 + renal impairment

***** 2 cases had insufficient data to categorise

181 patients developed 256 newly detectable post transfusion red cell alloantibodies. See Table 14.

Table 14
New post transfusion red cell alloantibodies 1996/97 - 2001/02
256 antibodies in 181 patients

Antibody group	Number	Sole antibody	
Kidd			
Jk[a]	78	49	
Jk[b]	19	11	(1 detected in eluate only)
Duffy			
Fy[a]	24	11	
Fy[b]	1		
Fy[3]	2		
Kell			
K	14	6	
Kp[a]	1		
Kp[b]	1	1	
Rhesus			
D	8	6	
C	8	1	
Cw	4		
c	21	6	
E	44	10	(1 reacting only by enzyme)
e	4	2	
MNSs			
M	4		
S	6	1	
s	2		
Lutheran			
Lu[a]	4		
Lewis			
Le[a]	1		
Other			
Yk[a]	1	1	
Anti B	1		
"private antigen" NOS[1]	1		
Wr[a]	1	1	
Chido	1	1	
A_1	1		
Bg	1		
P_1	1		
Unspecified pan-agglutinin	1		
Weak cold agglutinin	1		
TOTAL	**256**	**107**	

[1] Not Otherwise Specified

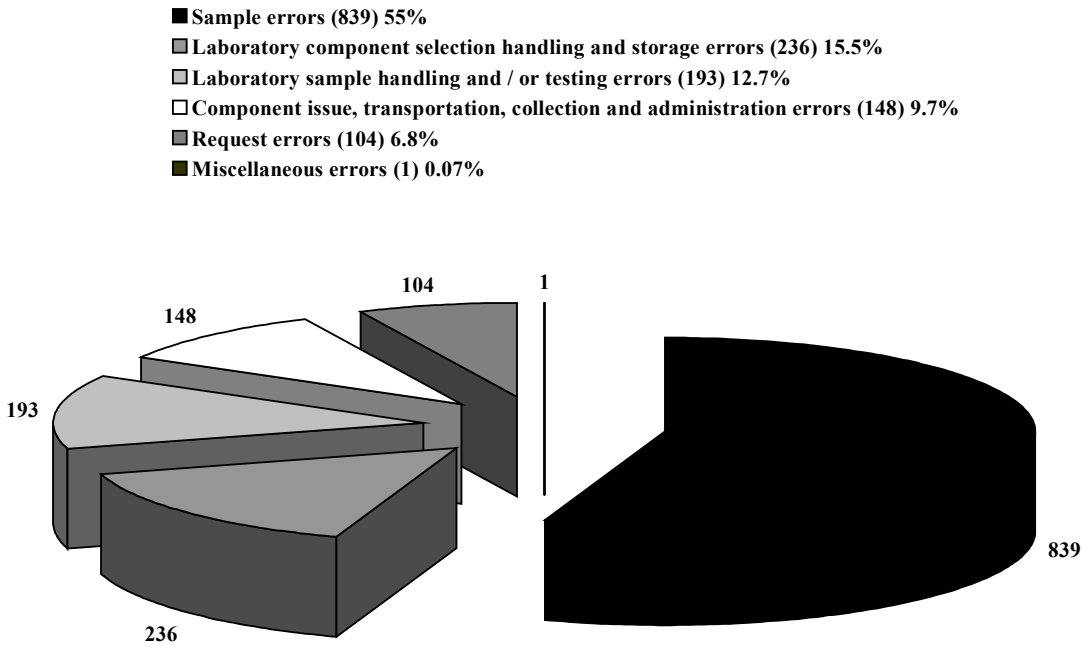
"Near Miss" Events 1997/98 – 2001/02

Data presented here are the cumulative figures for all "near miss" reports received since the scheme began. The scheme was piloted in time for the second reporting year (1997/98) and involved 4 hospitals over an 8 month period. In the following reporting year the scheme was expanded to include 22 hospitals over 7 months before being expanded again in 1999/2000 to include the same hospitals over a 12 month period. During the last two reporting years, all UK hospitals have been eligible to participate in the scheme.

Number of reports received 1521

Errors are listed in 6 categories as shown in the key to figure 17.

Figure 17
Categories of errors (n=1521)



7. THE CHIEF MEDICAL OFFICER'S NATIONAL BLOOD TRANSFUSION COMMITTEE

The Chief Medical Officer's National Blood Transfusion Committee in England was established in December 2001. It was created as a consequence of two major events in blood transfusion in the 1990s, the re-organisation of Blood Services in England, and the United Kingdom (UK) CMOs '*Better Blood Transfusion*' initiative. This short review will provide some background information about these developments presented in chronological order, and the initial work of the NBTC.

Establishment of the National Blood Authority and National Blood Service

The National Blood Authority was established in April 1993, and took over responsibility in England for what was previously known as the National Blood Transfusion Service in April 1994. This development sought to change a regionally based service into a national one. In September 1994, the NBA published its proposals for the future of the Regional Blood Transfusion Services, now to be called the National Blood Service. The proposals included the establishment of three administrative Zones to replace the previous regional structure. Many concerns were raised about these proposals during the consultation period.

When the Secretary of State finally approved the NBA's revised plans in November 1995, an independent National Blood Service User Group (NBUG) was set up to monitor the services provided by the NBS, to bring to the attention of the NBA problems which could not be resolved at local level, and to report annually to the Secretary of State. Zonal Blood User Groups (ZBUGs) were established in each of the 3 Zones of the NBS to inform the work of the National Blood Service User Group by seeking the views of those using the services provided by the NBS.

CMOs 1998 Blood Transfusion Seminar and Health Services Circular

In July 1998, the UK CMOs held a Seminar on '*Evidence-based Blood Transfusion*' in London attended by a multidisciplinary audience including blood users, representatives of Blood Services, NHS managers and patients. The factors leading to this initiative included concerns about the blood supply in the face of increases in the demand for blood and intermittent blood shortages, increases in the cost of blood associated with universal leucocyte-depletion of blood components and nucleic acid testing, data from the Serious Hazards of Transfusion (SHOT) scheme showing that the safety of transfusion should be improved, and concerns about the transmission of variant Creutzfeldt-Jakob disease (vCJD) by blood transfusion.

After wide consultation, the Health Services Circular '*Better Blood Transfusion*' (HSC 1998/224)[1] was issued in December 1998, and was based on recommendations from the Seminar. It detailed actions required of NHS Trusts and clinicians to improve transfusion practice, including the:-

- Establishment of a Hospital Transfusion Committee (HTC) to oversee all aspects of transfusion
- Participation in the SHOT scheme
- Development of agreed and disseminated local protocols for transfusion practice, based on national guidelines and supported by in-house training
- Consideration of the use of autologous transfusion, particularly peri-operative cell salvage

This was intended to be a first step towards safer and more effective blood transfusion in the NHS, and it was envisaged that the implementation of the recommended actions would be reviewed after about 2 years.

National management structure for the National Blood Service and the establishment of the National and Regional Transfusion Committees (RTC) in England

In 1999, the NBS Zones were integrated into a new national management structure for the NBS, and the ZBUGs were disbanded. There continued to be a need for a formal mechanism for interaction of the NBS with blood users, and it was proposed that Regional Transfusion Committees should be established. It was also proposed that a National Transfusion Committee be established to replace the NBUG on the lines of recommendations by the WHO Blood Safety Unit for national committees on the clinical use of blood. The remit of these committees would be primarily focused on improving transfusion practice in hospitals and supporting the implementation of the actions recommended in the Health Services Circular '*Better Blood Transfusion*'[1], although they would retain the role of the ZBUGs and NBUG in monitoring the performance of the NBS.

An Interim National Transfusion Committee met on three occasions in 2000/01 with the remit of establishing the Regional and National Transfusion Committee structure by September 2001. Its membership included the ex-Chairmen and blood bank members of the NBUG and ZBUGs, providing a useful link with the previous User Group structure, and also with the clinical membership of the National Commissioning Group.

CMOs 2001 Blood Transfusion Seminar and Health Services Circular

A second UK CMOs' Seminar on blood transfusion '*Better Blood Transfusion'* was held in London on 29th October 2001. It was again attended by an invited multidisciplinary audience. The objective of the Seminar was to set the agenda for NHS transfusion services for the next three years by seeking the views of the audience, focusing on:-

- Providing better information to patients
- Avoiding unnecessary transfusion
- Making transfusion safer
- Ensuring '*Better Blood Transfusion*' is an integral part of NHS care

After introductory remarks by the 4 UK Chief Medical Officers, the Chief Executive of the National Audit Office (NAO) summarised their report on the NBS, and how the NAO had organised the Seminar in collaboration with the Department of Health and the NBS. He challenged the NBS to describe how it is meeting hospitals' demands for blood, support and medical advice. Martin Gorham (Chief Executive, NBS) responded by outlining how the NBS was implementing the NAO's recommendations, and emphasised the support of the NBS for the *Better Blood Transfusion* initiative.
An audit of the implementation of the HSC 1998/224 *Better Blood Transfusion* was presented showing that most hospitals had established Hospital Transfusion Committees, participated in the SHOT scheme, and had protocols for the administration of blood. However, there was evidence of poor provision of training for clinical staff and patient information, few protocols for the appropriate use of blood, few audits of transfusion practice, and limited use of autologous transfusion.
Presentations were given by a patient on providing better transfusion services for patients, and by a representative of the Jehovah's Witnesses on methods for avoidance of blood transfusion. How to make blood transfusion safer was discussed by representatives of the National Patient Safety Agency (NPSA) and SHOT. The final sessions of short presentations were on how to improve the quality of transfusion practice and how to make HTCs more effective. In the afternoon, the audience participated in 5 workshops on:-

- The needs of people at risk of transfusion
- Making blood transfusion safer
- National blood transfusion protocols
- Monitoring the use and effectiveness of blood transfusion
- Strengthening the HTC and the role of the Transfusion Nurse Practitioner

The main points from each workshop were presented to the whole audience in a final discussion led by the CMOs. The establishment of the CMO's National Blood Transfusion Committee and Regional Transfusion Committees in England was announced at the Seminar. Recommendations from the work carried out at the Seminar were published in a Health Services Circular *Better Blood Transfusion – Appropriate Use of Blood* (HSC 2002/009)[2] in July 2002. These included an action plan and an ongoing programme for *Better Blood Transfusion* to be taken forward in each Trust.

Initial meetings and work of the CMO's National Blood Transfusion Committee in England

The NBTC held its first meeting on 3rd December 2001. Professor E.Gordon-Smith, who was the Chairman of the National Blood User Group and the Interim National Transfusion Committee, was appointed Chairman by the CMO. The NBTC membership includes the Chairmen of the Regional Transfusion Committees, and representatives of the Royal Colleges, SHOT, NPSA, NBS, patients, and the Department of Health. Its primary remit is to support the *Better Blood Transfusion* initiative. It is envisaged that there should be a two-way flow of information between Hospital Transfusion Committees and the Regional and National Transfusion Committees to encourage good local blood transfusion practice and implement national transfusion guidelines. In addition, the identification of problems in any aspect of blood transfusion including the delivery of services by the National Blood Service remains within the remit of the Regional and National Committees.

There are two meetings of the NTBC each year. The work of the committee between meetings is carried out by an Executive Working Group comprising the Chairman, 5 members of the committee, two National Blood Service representatives, a patient representative and a representative from the Department of Health.
The work of the NBTC in 2002 focused on providing the 'toolkit' to assist Trusts in their implementation of the Health Services Circular *Better Blood Transfusion*. This has included the development of a revised version of the patient information leaflet for blood transfusion, a summary of indications for the use of blood components abstracted from national guidelines, and a document on the *'Resources required to implement Better Blood Transfusion'* (appendix 9). This document was intended to help HTCs develop a business case for:-

- The establishment of a Hospital Transfusion Team in each Trust, particularly for the role of Transfusion Practitioners, dedicated sessions for a lead Consultant in blood transfusion, and for audit and administrative support
- Information technology support for data retrieval for audit and participation in the Blood Stocks Management Scheme
- Clinical equipment e.g. for cell salvage, computerised blood refrigerator monitoring
- Funding of other alternatives to the use of donor blood, as determined by the clinical activity and priorities in each Trust

The NBTC also produced a discussion document on *'The use, availability and risks of fresh frozen plasma'*. This recognised that the indications for the use of fresh frozen plasma were last drawn up by the British Committee of Standards in Haematology in 1992 (and are currently being revised by the BCSH), and that audits of the use of FFP show variable compliance with the guidelines and some inappropriate use of FFP[10]. The main concerns about the use of FFP were thought to be viral transmission, the risk of transmission of vCJD, and transfusion-related acute lung injury. The NBTC considered that the most important requirements to enhance its safety were:-

- Viral inactivation steps of proven effectiveness should be applied to FFP.
- Donations should be sourced from low risk vCJD populations.
- Donations should only be taken from male, untransfused donors if single unit preparations are used. Pooled products may also be used to avoid TRALI.

The NBTC translated these requirements into the following recommendations for consideration by the Department of Health Advisory Committee on the Microbiological Safety of Blood and Tissues for Transplantation (MSBT) at its meeting on 22nd October 2002:-

Single unit, virally inactivated, donations from non-UK, untransfused males, should be used for most vulnerable groups (i.e. infants born after January 1996). An announcement had already been made by the Department of Health in August 2002 about the importation of FFP from the United States for single unit methylene blue-treated FFP for infants born after January 1996. The primary motivation for this initiative was to protect those individuals who had not been exposed to Bovine Spongiform Encephalopathy-contaminated beef from the possible exposure to vCJD from UK blood.

- Pooled, virally inactivated (by proven and preferably licensed methods) donations from populations at low risk of transmissible spongiform encephalopathy are acceptable.
- Untreated single donor or UK sourced products should only be permitted (a) if products from other sources cannot meet demand, (b) they are used in the least vulnerable group of recipients (i.e. older populations who will receive only a single or small number of treatments). Of these two considerations the first, i.e. non-availability of product from other sources, is the main consideration.

The NBTC has also established a Working Party on Information Technology (Chair: Dr.C.Morgan) with a remit to:-

- Collate information on projects directed at improving the safety and effectiveness of transfusion practice through the use of IT.

- Make recommendations on how to make best use of IT for improving transfusion practice, including the safety of the clinical transfusion process, appropriate use of blood, and the documentation of transfusion.

- Establish key standards and principles for clinical transfusion IT systems, including functionality, connectivity, security and confidentiality. Transfusion systems should integrate with the development of other hospital-based systems such as pharmacy, pathology and electronic patient records.

- Make recommendations on the development of IT links between hospital blood banks, users of their services in hospitals and primary care, and the NBS.

- Stimulate further progress in the use of IT for hospital transfusion practice, including consideration of new projects to further the field, and the provision of appropriate access to funding through NHS R & D, Health Technology Assessment, and Modernisation of Pathology initiatives.

- Work with other organisations involved in improving transfusion practice, including commercial suppliers.

The membership of this Working Group includes representatives from the NBTC, British Society for Haematology, National Patient Safety Agency, NHS Information Authority, Department of Health Information Policy Unit, UKBTS/NIBSC Standing Advisory Committee on IT, Specialist Practitioners of Transfusion (SPOT), Institute of Biomedical Sciences, and the NBS.

Further information about the terms of reference, membership, and work of the NBTC can be obtained from the Secretary, Dr.M.Murphy (National Blood Service, John Radcliffe Hospital, Oxford), from the Chair of the appropriate RTC or from the NBTC website http://www.doh.gov.uk/blood/nbtcommittee.htm. The website for the *Better Blood Transfusion* initiative is http://www.doh.gov.uk/blood/bbt.htm.

M.F.Murphy
Lead Consultant for Hospital Liaison, NBS, Secretary to National Blood Transfusion Committee

E.A.E.Robinson
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Chairman of National Blood Transfusion Committee

12.3.03

8. HOW HAS THE SHOT REPORT AFFECTED MY WORKING DAY? A BIOMEDICAL SCIENTIST'S PERSONAL VIEW

The biomedical scientist has been at the forefront of many developments in the field of blood transfusion safety. The expertise and experience that has always been an integral part of the BMS approach to blood transfusion practice has been the cornerstone of many such developments. This important contribution to progress in transfusion medicine has almost certainly been under-recognised in the past. However with the publication of the first SHOT report 6 years ago things began to change. Areas of concern that had been flagged up by laboratory staff for many years were now seen to be 'real' and the eyes of the hospitals management began to focus on these risk areas with a new enthusiasm. The SHOT report was about to have the most major impact on clinical and laboratory blood transfusion practice since the development and introduction of the Antiglobulin Test 60 years earlier.

The role of the BMS working in a blood transfusion laboratory, whether this be in a hospital or a blood centre, encompasses several areas where real risks exist in the provision of a safe, appropriate and beneficial product for clinical treatment of the patient. These areas of action and involvement are listed below. The list is by no means exhaustive.

- Obtaining the sample from the patient
- Correct labelling of sample and request in the laboratory
- Correct entry of patient demographics onto IT system
- Production of safe clinically effective blood components
- Selection of appropriate blood / component
- Control over the appropriate use of anti-D IgG (antenatal and postnatal)
- Monitoring blood use and developing maximum blood order schedules for routine procedures
- Correct and valid use of laboratory systems for grouping, antibody screening and crossmatch
- Correct labelling of blood / components prior to issue
- Ensuring correct product is collected for a given patient
- Ensuring full audit trails exist for all clinical products and procedures
- Ensure correct storage of all clinical products and reagents
- Ensure competency of all staff undertaking work in the laboratory is maintained.
- Ensure that there is full quality monitoring of all processes undertaken
- Liaison with nursing and medical staff
- Risk assessment of all processes
- Development of novel ways to minimise risk including IT solutions to patient identification problems and development of cell salvage programmes.
- Giving advice concerning the technical aspects of blood transfusion practice and more recently helping provide clinical advice in discussion with the Consultant Haematologist.
- An advisor where transfusion protocols are being developed e.g. appropriate use of emergency O RhD negative blood, management of massive haemorrhage.
- Education of staff whose role is primarily in other areas of the transfusion process.

All these things have seen the role of the BMS change immeasurably over the last 5 years and many senior BMSs are now taking a lead role in the development of safe practices within their hospital.
Although hospital transfusion committees have been operating for 10 years or more in some hospitals many more are only just seeing the benefits of such a committee. The initial driving force for the establishment of many HTCs came from the Consultant Haematologist and the lead BMS in Blood Transfusion. Indeed the lead BMS was and still is in many instances the driving force in the running of these committees and in the implementation of decisions taken. The days of the lead BMS in blood transfusion being surrounded by tubes, cell washers and packs of blood are numbered and in many cases have already gone. The lead BMS is now a very influential cog within the wheel of hospital transfusion practice and helps to shape the future provision of this service in a way which that have been unthinkable 15 years ago.

It was very obvious 20 years ago that the requirement for the provision of blood products in hospitals was increasing rapidly and stretching the resources of the laboratory in such a way that novel approaches needed to be developed in order to maintain a safe service in the face of ever increasing demands. This heralded the heyday of microplate technology and the more widespread use of computer technology for managing the security of the process. In the 1980's it was the grouping, antibody screening and crossmatching processes that

were encompassed in this brave new world. However, it would not be long before the expertise gained by laboratory staff would be channelled into developing more sophisticated means of providing a totally secure system for the delivery of clinically appropriate blood components into the right patient at the right time.

Despite the fact that we knew that blood transfusions could transmit infections e.g. Hepatitis B there came the first real scare over blood transfusion and infection in the 1980's - the HIV crisis. This focused the professions' attitude to the appropriate use of blood but it was not until some years later that our attention was really grasped. Hepatitis C infection followed by the unknown risk of vCJD made all of us sit up and take notice – there would have to be changes in practice to minimise the risk of adverse events and to safeguard potentially scarce blood supplies. Biomedical scientists had, for many years, sought support for controlling the use of blood components but it had proven difficult to influence old habits of transfusion therapy at the bedside. New research into blood transfusion and clinical outcomes supported by publications such as the SHOT report were to prove invaluable in educating clinicians and others to the need to change practice.

Laboratory staff have always placed emphasis on the importance of recording errors and acting to reduce them but errors which were initiated either before receipt of sample and request into the laboratory or at the bedside, were often not recognised. The SHOT report has highlighted the need for a holistic approach to blood transfusion practice where ALL staff involved take responsibility for their own actions and for the provision of a safe and appropriate clinical service that is subject to regular audit and improvement in all areas. The expertise and knowledge of BMSs has been invaluable in the initiation of such an approach.

The SHOT report has highlighted a number of things (see list below) which have subsequently been documented in Better Blood Transfusion 1 and 2. These, coupled with the Clinical Negligence Scheme for Trusts have proved to be the prime movers for improvement.

- We, all hospitals, share the same problems
- Education and training are the biggest areas of concern
- There is a need to embrace a 'blame free' error reporting culture which will lead to real improvements in the safety of the process
- Lack of audit leads to complacency
- There is a need to benchmark practice in all areas of the process
- Risk assessments need to be undertaken
- The need for clinicians to take a more responsible line when ordering and using blood components.

Not only do we have a problem with guaranteeing the future supply of blood components but the SHOT reports have also highlighted serious flaws in the service that we are providing. A series of recommendations have appeared in SHOT reports over the last 6 years which are directed at improving the safety, appropriateness and clinical benefit to the patient. This has had a dramatic effect on the role of the BMS at all levels but most notably on those staff leading the laboratory service.

Within the laboratory the SHOT initiative has highlighted the need for

- comprehensive IT systems
- adequate staffing
- automation
- training
- audit

Within the ward and theatre environment SHOT has recommended

- more secure means of patient identification
- appropriate ordering and use of blood components as indicated by national guidelines
- development of autologous blood provision whether by means of pre-operative donation, acute normovolaemic haemodilution, intraoperative cell salvage or post operative cell salvage
- more attention to monitoring and recording of transfusion episodes
- more attention to recognition of transfusion reactions

The traditional view of a transfusion laboratory worker as a bearded eccentric clothed in a white coat, living in

the bowels of pathology and interested only in the identification of complex antibody combinations has been left behind in the 20th century. Today's transfusion laboratory staff are at the forefront of change. All the recommendations mentioned above have become the remit of the hospital transfusion committee and in many instances specifically the remit of the lead BMS. In helping to drive forward radical improvements in laboratory and clinical practice laboratory staff are shaping the vision for the future by implementing recommendations from SHOT reports. The arrival of SHOT has given BMSs a route to follow and the backing needed in order to realise their full potential in the organisation as trainers, auditors, innovators, advisors and achievers within the field of blood transfusion medicine. Today's BMS in the blood transfusion laboratory has the potential to become the Specialist Practitioner of transfusion that all trusts are bound to have as part of their hospital transfusion team in accordance with "Better Blood Transfusion"[1, 2]

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9. IMPROVING TRANSFUSION PRACTICE – THE ROLE OF AUDIT

Why audit transfusion practice?

The SHOT scheme has shown that avoidable, serious hazards of transfusion continue to occur in Trusts, the most common being giving the wrong blood to patients. The incidents reported are frequently due to failure of the bedside check, often compounded by other errors earlier in the transfusion chain. Blood must be used appropriately, as well as safely, to conserve the scarce blood supply for those who need it most, whilst ensuring that others are not unnecessarily exposed. Blood should only be used when clinically indicated. Clinical audit is a useful tool to monitor and improve practice against agreed guidelines, looking at both the transfusion process and appropriateness of transfusion

The national audit process and Better Blood Transfusion initiative

In 1995, the National Health Service Executive funded a national audit initiative run by the Royal College of Physicians (RCP) Clinical Evaluation and Effectiveness Unit looking at blood transfusion practice and documentation in hospitals (Murphy et al, 2001). This process together with the SHOT findings led to the development of a guideline for hospitals on blood administration (BSCH, 1999) and the issue of Health Service Circulars (HSC) on Better Blood Transfusion in 1998 and 2002 (HSC 1998/224; HSC 2002/009). A national comparative audit of red cell transfusion is currently underway, under the auspices of the National Blood Service and Clinical Effectiveness and Evaluation Unit of the RCP (doh.gov.uk/bbt2/lettertoce.htm). The audit is in three stages: i) audit of hospital transfusion policy, ii) audit of bedside transfusion practice and iii) audit of appropriate use of blood (currently in planning phase). It is hoped that there will be improvement in practice through utilising comparative data in a benchmarking system. Each participating hospital receives a report of their practice within 14 days of returning their data with a comparative report planned for July 2003. The Specialist Practitioners of Transfusion group have also recently completed an audit of bedside transfusion practice, results of which will be fed back to participating trusts and in a national report in mid 2003.

HSC 2002/009 Better Blood Transfusion endorses participation in audit and strengthens the role of the Hospital Transfusion Committee via the Hospital Transfusion Team to ensure that blood transfusion is appropriate and safe through implementation of transfusion policies based on national guidelines, education and training, and participation in the SHOT scheme. The establishment of Regional and National Transfusion Committees will support the process through their remit to support the HTCs in promotion of good transfusion practice. The NBS clinical audit department, accessed via hospital liaison consultants, can provide advice on audit planning, provision of audit tools and dissemination of good practice. Three annual clinical audit and effectiveness conferences have been held.

The audit process

The aim of clinical audit is to improve effectiveness and efficiency of medical care (Fowkes, 1982). Achieving this aim should involve a cycle of activities: i) observing practice ii) setting standard of practice iii) comparing the observed practice with the standard iv) implementing change v) re-observing practice. Audits can be conducted prospectively, concurrently or retrospectively. The prospective approach can be used to monitor the appropriateness of requests for transfusion but can potentially delay the delivery of improvements in patient care. Concurrent audit of component utilisation does not immediately prevent unnecessary transfusion but if conducted in a timely and individual fashion can provide effective educational feedback resulting in change of practice. Comparison of transfusion practice within or between hospitals is a form of retrospective audit and if linked to effective educational programmes can be a powerful tool for persuading clinicians to change their practice.

In order for audit to be successful, the cycle must be completed: i) the results and educational messages must be disseminated and discussed by those whose practice could be improved ii) analysis of corrective actions required to improve practice and iii) provision of resources to implement the actions identified.

The burden imposed by clinical audit on the already onerous workload of haematologists and blood bank staff should not be underestimated and needs to be allowed for in manpower planning. Specialist practitioners of transfusion can provide much needed support for audit and monitoring in addition to their role in education and training.

Audit of the transfusion process

The BCSH guideline on administration of blood and blood components and the management of transfused patients (BCSH, 1999) is the current standard for use in auditing the transfusion process and forms the basis of the current national comparative audit. The successive SHOT reports highlight problem areas where audit needs to concentrate: the bedside check, the use of wrist bands, prescribing of blood including special requirements, telephone requesting, collection of blood from storage refrigerators, phlebotomy standards and laboratory errors.

The transfusion process can be monitored by a combination of logging of actual errors and near misses and direct observation. Galloway et al (2002) reported on a system developed to provide feedback to users on unacceptable practice in the delivery of transfusion (figure 18). Adverse events were logged and scored according to the seriousness of the event. Each incident was investigated and lessons learnt implemented via the HTC through changed in hospital policy or laboratory Standard Operating Procedure (SOP)s. Cumulative scores were fed back to the staff and high scoring areas were investigated in more detail. Feedback raised the profile of transfusion safety in the organisation. This system of error logging was not good at detecting errors between the point of blood issue and transfusion. The best method of detecting errors in this area is by direct observation (Whitsett and Robichaux, 2001). This method is labour intensive but can be very effective when used in combination with error logging to target problem areas. The national comparative audit is based on direct observation at the time of transfusion with some information being collected once the transfusion is completed.

Galloway et al (1999) have also used error logging to monitor laboratory performance. Twenty-eight percent of wrong blood incidents in the first 6 years of the SHOT scheme have been attributed to laboratory errors. Galloway et al divided errors into pre-analytical, analytical and post-analytical and information was collected prospectively. All errors were fully investigated and reported to the HTC. The majority were pre-analytical; associated with incomplete data on sample or request form (10% of procedures), including 3 examples of wrong blood in sample tube. There were also analytical errors (5.8% of procedures) mainly due to transcription errors in the laboratory and post-analytical errors (0.5% of procedures) due to failure to follow procedure for component collection. Most of the errors were near-miss events. It is hoped that the SHOT system of "near miss" event reporting will allow for benchmarking of performance between laboratories.

Clark et al (2001) have audited the effect of a formal education programme on the safety of blood transfusion practice. A baseline audit of the transfusion process by direct observation and case note review plus questionnaire on knowledge of guidelines was undertaken. An education package was developed and disseminated by Transfusion Nurse Specialist and included study days, self-directed clinical skills package and cascade training. A follow up audit showed an improvement in compliance with BCSH guidelines and the programme is now being rolled out across several acute Trusts in Scotland.

Audit of the appropriateness of transfusion

Blood should only be used when clinically indicated on the grounds of cost, effectiveness and availability. Clinical audit can monitor and improve practice against agreed guidelines. Phase 3 of the national comparative audit will be looking at the appropriateness of transfusion.

- ***Where does the blood go?***
  There have been 2 population based studies undertaken (Stanworth et al, 2002; Wells et al, 2002) on red cell usage. These studies identify the major users of blood that can be targeted for audit of appropriateness of usage. The Newcastle study (Wells et al, 2002) showed 51.6% blood transfused for medical indications and 47% for surgical indications. The London study (Stanworth et al, 2002) found 51.2% transfused for surgical indications and approximately 40% for medical indications. In the latter study, 8% of blood was not traceable due to deficiencies in hospital computer systems. Haematologists, orthopaedic surgeons and general surgeons were the biggest users.
- ***Indications for transfusion***
  Indication codes for transfusion have been prepared as part of the tool kit for Better Blood Transfusion, based on UK national guidelines for the use of blood and blood components (appendix A). It is hoped that this information will help clinicians decide when transfusion is appropriate alongside clinical judgement. The codes can be used when requesting blood and will be useful for audit purposes.
- ***Red cell transfusion***
  Wallis et al (2002) have written an excellent review on audit of red cell transfusion. Audits of the transfusion trigger, compliance with maximum surgical blood order schedule (MSBOS), discharge haemoglobin (Hb), recording of minimum data set (indication, outcome, adverse events, documentation of date and pack number) can all be used to analyse appropriateness of transfusion. Comparative audits have shown large variations in red cell use (Sirchia, 1994) and feedback of the information to users together with

an education package can result in reduction of blood use in for example orthopaedic (Welsh scheme, D Thomas personal communication) or cardiac surgery (Struck et al, 1990). Audit of discharge Hb rather than the number of units transfused may be a better indicator of best practice. Elective surgery is a common target for audit, but transfusion of medical patients is coming under increasing scrutiny although there is very little published in this area. Various groups have demonstrated reduction in red cell use in elective surgery following introduction of a transfusion trigger (Torella et al, 2002; Mallet et al, 2000) of between 8-10 g/dL. Use of near patient testing may aid decisions to transfuse in theatre. James et al (2001) have demonstrated the impact of a 10 year audit cycle on improving blood usage in a District General Hospital, looking at blood use by consultant, surgical procedure using crossmatch: transfusion ratio, revision of MSBOS, problem areas and non-surgical setting with benchmarking and feedback.

- ***Fresh frozen plasma (FFP) transfusion***
  The SHOT scheme reports higher rate of adverse events with platelet and FFP transfusion compared to red cells. A national audit of FFP use was initiated in June 2001 (Stainsby and Burrowes-King, 2002) and looked at where and why components were used and what strategies were being put in place to reduce inappropriate use. It is hoped to extend this to a national benchmarking and comparative audit of FFP use. In the first phase, only 49% of trusts responded to the questionnaire and of these, 53% had policies for FFP use in place. Six local audits submitted showed compliance with BCSH guidelines of 62% - 92%. Clinical notes and blood bank requests were frequently found to be inadequate for assessment. Recommendations for the first phase suggested that local strategies should be put in place by HTCs to cover: policies and educational programmes, audit and monitoring, educational request forms, accurate documentation and implementation of dose-weight chart.
- ***Platelet transfusion***
  There is little published literature in this area. Callow et al (2002) have looked at the frequency of bleeding complications in patients with haematological malignancy following introduction of a stringent prophylactic platelet transfusion policy based on the RCP consensus conference statement (Contreras, 1998). They showed that the introduction of the transfusion trigger of 10 x 109/L in absence of fresh bleeding is safe and has significant impact on hospital transfusion costs.

Conclusion

Audit of both the transfusion process and appropriateness of transfusion should be an integral part of the work of a hospital and its blood bank. The SHOT scheme provides information to allow for targeting of problem areas, particularly in the transfusion process. Audit requires significant input of medical, nursing, laboratory and clerical time and is supported by the Better Blood Transfusion initiative. Audit must be backed up by effective education programmes and systems of continuous improvement to ensure change of practice. Better Blood Transfusion needs to be adequately resourced, otherwise SHOT 5 years on will show no change.

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Appendix A

INDICATION CODES FOR TRANSFUSION – AN AUDIT TOOL

The indications for transfusion provided below are taken from UK national guidelines for the use of blood components (see references). Although it is accepted that clinical judgement plays an essential part in the decision to transfuse or not, the purpose of drawing available transfusion guidelines together into one short document is to help clinicians decide when blood transfusion is appropriate, and to minimise unnecessary exposure to transfusion.

Each indication has been assigned a number, which may be used by clinicians when requesting blood or for purposes of audit. Specific details regarding the patient's diagnosis and any relevant procedures to be undertaken should also be provided.

These are current guidelines and may change depending on new evidence.

Red cell concentrates

R1. *Acute blood loss* (British Committee for Standards in Haematology, 2001):-

Objective: to maintain circulating blood volume and haemoglobin (Hb) concentration > 7 g/dl in otherwise fit patients, and > 9g/dl in older patients and those with known cardiovascular disease.

15-30% loss of blood volume (800-1500ml in an adult): transfuse crystalloids or synthetic colloids. Red cell transfusion is unlikely to be necessary.
30-40% loss of blood volume (1500-2000ml in an adult): rapid volume replacement is required with crystalloids or synthetic colloids. Red cell transfusion will probably be required to maintain recommended Hb levels.
>40% loss of blood volume (>2000ml in an adult): rapid volume replacement including red cell transfusion is required.

***Peri-operative transfusion* (Association of Anaesthetists, 2001; British Committee for Standards in Haematology, 2001; Scottish Intercollegiate Guidelines Network, 2001):-**

Many patients undergoing elective surgical operations should not require transfusion support if their Hb concentration is normal before surgery. Assuming normovolaemia has been maintained, the Hb can be used to guide the use of red cell transfusion.

R2. Hb concentration below 7g/dl.
R3. Hb concentration below 9 g/dl in a patient with known cardiovascular disease, or those with significant risk factors for cardiovascular disease (e.g. elderly patients, and those with hypertension , diabetes mellitus, peripheral vascular disease).

***Critical Care* (British Committee for Standards in Haematology, 2001);**

R4. Transfuse to maintain the Hb >7g/dl.

Post-chemotherapy

R5. There is no evidence-base to guide practice. Most hospitals use a transfusion threshold of a Hb of 8 or 9g/dl.

Radiotherapy

R6.Transfuse to maintain Hb above 10g/dl.

***Chronic anaemia* (British Committee for Standards in Haematology, 2001):-**

R7. Transfuse to maintain the haemoglobin just above the lowest concentration which is not associated with symptoms of anaemia. Many patients with chronic anaemia may be asymptomatic with a haemoglobin concentration >8g/dl.

Fresh frozen plasma (British Committee for Standards in Haematology, 1992)

(Dose - 12-15 ml/kg body weight equivalent to 4 units for an adult)

F1. Replacement of single coagulation factor deficiencies, where a specific or combined factor concentrate is unavailable e.g. factors V.
F2. Immediate reversal of warfarin effect, in the presence of life-threatening bleeding.
F3. Acute disseminated intravascular coagulation (DIC) in the presence of bleeding and abnormal coagulation results.
F4. Thrombotic thrombocytopenic purpura (TTP), usually in conjunction with plasma exchange.

F5. Massive transfusion, coagulation factor deficiency can be expected after blood loss of 1.5 x blood volume, aim for PT & APTT < 1.5 of the control value.
F6. Liver disease, to correct bleeding or as prophylaxis before surgery when the prothrombin time is >1.5 the control value.

Cryoprecipitate
(Dose - 1 unit/5kg body weight equivalent to 10 units for an adult)
C1. Acute disseminated intravascular coagulation (DIC), where there is bleeding and a fibrinogen level < 1g/l.
C2. Advanced liver disease, to correct bleeding or as prophylaxis before surgery, when the fibrinogen level <1g/l.
C3. Bleeding associated with thrombolytic therapy causing hypofibrinogenaemia.
C4. Hypofibrinogenaemia (fibrinogen level <1g/l) secondary to massive transfusion
C5. Renal failure or liver failure associated with abnormal bleeding where DDAVP is contraindicated or ineffective

Platelet concentrates (British Committee for Standards in Haematology, 1992; Consensus Conference on Platelet Transfusion, 1998; Schiffer et al for the American Society of Clinical Oncology, 2001)
(Dose - 15 ml/kg body weight equivalent to 1 adult therapeutic dose for an adult)
Bone marrow failure
P1. To prevent spontaneous bleeding when the platelet count <10 x 10^9/l.
P2. To prevent spontaneous bleeding when the platelet count <20 x 10^9/l in the presence of additional risk factors for bleeding such as sepsis or haemostatic abnormalities.
P3. To prevent bleeding associated with invasive procedures. The platelet count should be raised to >50 x 10^9/l before lumbar puncture, epidural anaesthesia, insertion of intravascular lines, transbronchial and liver biopsy, and laparotomy, and to >100 x 10^9/L before surgery in critical sites such as the brain or the eyes.

Critical care/surgery
P4. Massive blood transfusion. The platelet count can be anticipated to be <50 x 10^9 /l after 1.5-2 x blood volume replacement. Aim to maintain platelet count >50 x 10^9 /l.
P5. Bleeding, not surgically correctable and associated acquired platelet dysfunction e.g. post-cardiopulmonary bypass, possibly combined with the use of potent anti-platelet agents such as clopidigrel.
P6. Acute disseminated intravascular coagulation (DIC) in the presence of bleeding and severe thrombocytopenia.
P7. Inherited platelet dysfunction e.g. Glanzmanns thrombasthenia with bleeding or as prophylaxis before surgery.

Immune thrombocytopenia
P8. Autoimmune thrombocytopenia, in the presence of major haemorrhage.
P9. Post-transfusion purpura, in the presence of major haemorrhage.
P10. Neonatal alloimmune thrombocytopenia, to treat bleeding or as prophylaxis to maintain the platelet count >50 x 10^9 /l.

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Prepared by MF Murphy and JP Wallis October 2002 for National Blood Transfusion Committee

Figure 18

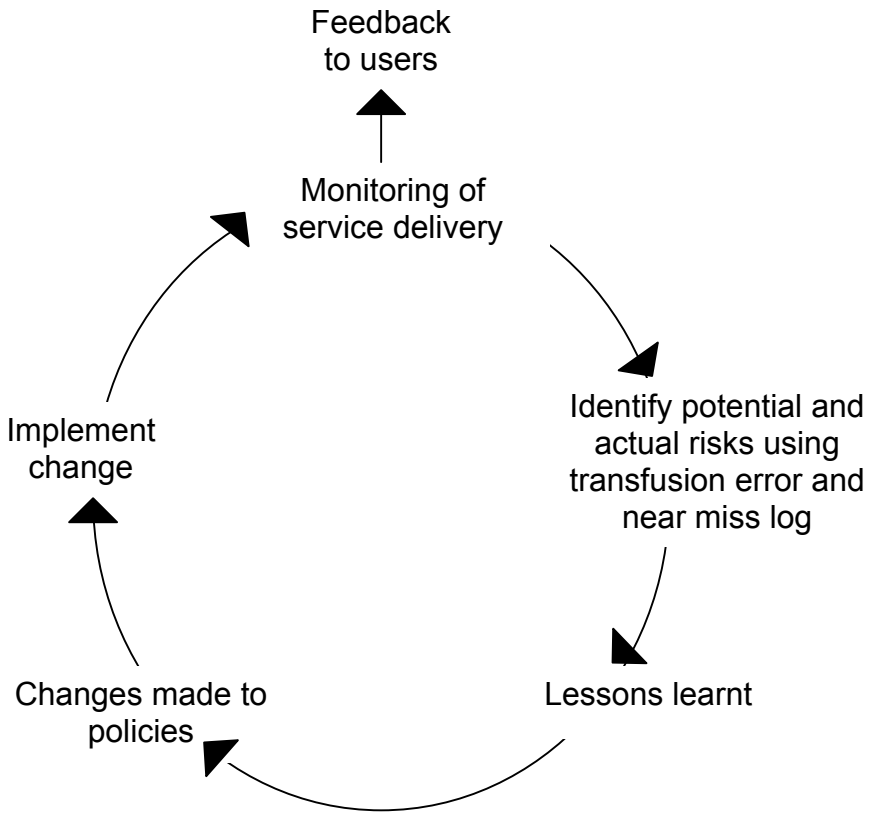


Figure 18
Outline description of the quality improvement process developed to provide feedback on performance to users of the hospital transfusion service (taken from Galloway et al 2002).

Galloway M, Woods R, Whitehead S and Gedling P, (2002) *Providing feedback to users on unacceptable practice in the delivery of a hospital transfusion service – a pilot study*. Transfusion Medicine, **12**, 129-132

10. INCORRECT BLOOD COMPONENT TRANSFUSED

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

As in all previous years this category represents the highest number of reports received. For the 12 month period, Oct. 2001-Sep. 2002, 258 new initial reports were received, and a total of 343 to the end of the new reporting year (December 2002). This is a 21.1% increase over the equivalent 12 month reporting period 2000-2001 and IBCT reports comprise 71.7% of all reports received. There is therefore a continuing steep rise in the number of IBCT reports being received, indicating a significant degree of underreporting in the past and increasing awareness and confidence in the SHOT scheme. This chapter analyses 346 completed questionnaires, including 27 which were outstanding from the preceding year. Completed questionnaires are outstanding on 25 initial reports and will be analysed next year. In addition, 15 reports were withdrawn as not meeting the criteria for IBCT and 10 have been "written off" due to failure to submit a completed questionnaire within an appropriate timescale.

Analysis of reported errors

The questionnaires sought further information about the circumstances and factors which may have contributed to errors and adverse outcomes. The findings are presented in some detail with the use of case studies where appropriate. The aim is to illustrate weak points in the transfusion process in order to help those responsible for training staff, or for the review and implementation of transfusion procedures, to identify areas for improvement and so ensure that the right blood is given to the right patient at the right time.

The data from 346 completed questionnaires are presented.

The following 3 tables give information on the gender, age of recipients and the blood components implicated in the incident.

Table 15
Sex of IBCT patients

Female	=	189
Male	=	154
Unknown	=	3
Total	=	**346**

Table 16
Age of IBCT patients

Age of recipients	
Age range	0 to 98 years
Median Age	51 years

Table 17
Components implicated in IBCT (356 components in 346 cases)

Components implicated	Number of cases
Red cells	252
Platelets	36
Fresh Frozen Plasma	19
Cryoprecipitate	2
Anti-D immunoglobulin[1]	44
Other [2]	3

[1] Adverse events to this plasma product are usually reported through the MHRA yellow card system but these incidents are reported here because they fall into the category of either blood derivative to the wrong patient or unnecessary administration of a blood derivative due to an error earlier in the chain.

[2] 1 x granulocytes, 1 x expired albumin, 1 x Human Factor VIII

It is clear that errors occur in the transfusion of patients of all ages and in the administration of all types of components.

The outcome of 346 fully analysed incidents is shown in table 18

Table 18
Outcome of 346 fully analysed incidents

OUTCOME	NO. OF INCIDENTS
Death definitely related to transfusion	0
Death probably related to transfusion	1
Death possibly related to transfusion	3
Death unrelated to transfusion	18
Major morbidity*	9
Minor or no morbidity	310
Outcome unstated by reporter	5

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

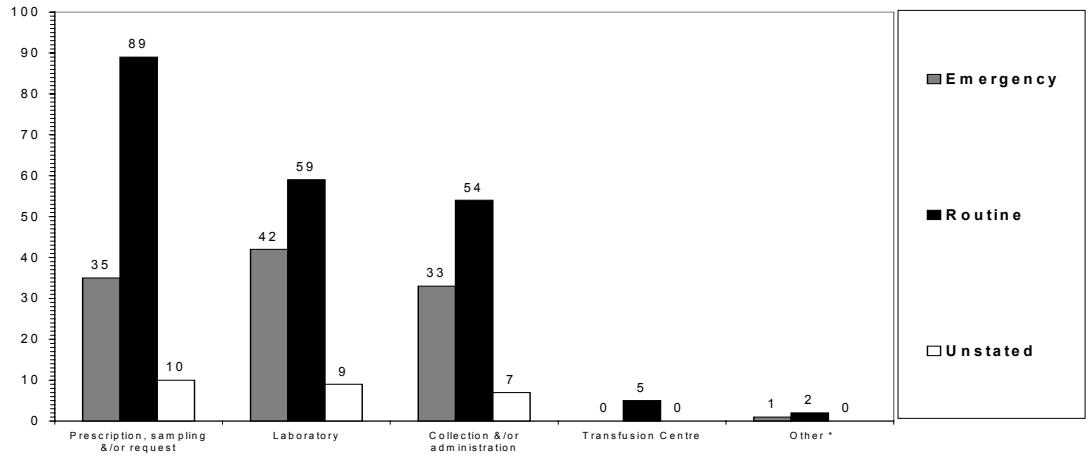
- Intensive care admission and/or ventilation
- Dialysis and/or renal impairment
- Major haemorrhage from transfusion-induced coagulopathy
- Intravascular haemolysis
- Potential risk of RhD sensitisation in a female of child-bearing potential

As in previous years, the small numbers of deaths belies the potential for a disastrous outcome in many of the incidents reported and major morbidity was reported in only 2.6% of cases.

Emergency and elective transfusions

Of the 346 completed questionnaires, 209 (60%) related to elective and 111 (32%) to emergency transfusions. These proportions are similar to those noted in previous years but we lack denominator data to determine whether or not emergency transfusions pose a greater risk of error than elective transfusions. It is perhaps surprising that 60% of errors occur in an elective setting. Twenty-six questionnaires did not state whether the transfusion was elective or emergency. Figure 19 shows the distribution of errors relating to emergency and elective transfusions.

Figure 19
Incidence of errors at the various stages of the process of emergency and elective transfusion (n=346)



*

Other = 3 x blood bank refrigerator failure

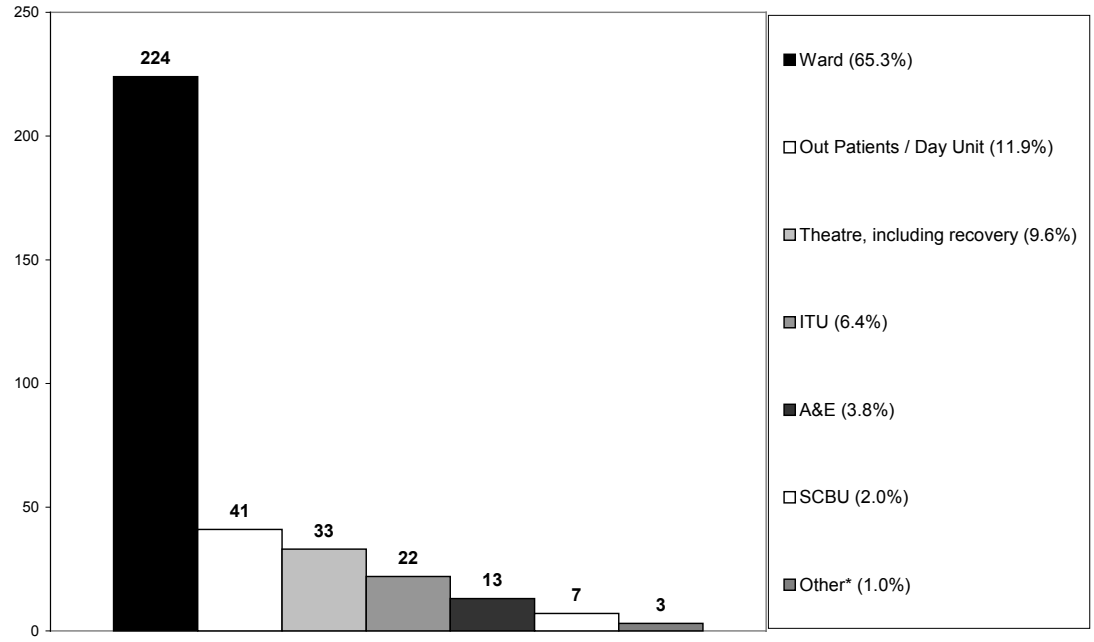
Respondents were also asked whether or not the transfusions took place during normal working hours or outside normal working hours. While we currently lack denominator data on this aspect of transfusion the responses are still of interest. Modifications to all questionnaires are now in progress in order to collect more detailed information on the potential impact of "out-of-hours" working on laboratory and clinical transfusion practices.

- 165 transfusions took place in normal working hours (47.7%)
- 156 were outside normal working hours (45%)
- 6 reporters stated both normal and outside normal working hours (1.7%)
- 4 reporters stated that they did not know the answer to this question (1.2%)
- 15 reporters did not respond (4.3%)

Site of transfusion

The questionnaire asked for information about where the transfusion took place. Three hundred and forty-three reports gave information on the site of the transfusion (figure 20). Again, this information is of limited value, as no denominator data are available. However, it is notable that 11.9% of incidents took place in out-patient or day case settings where use of name-bands is less common than in in-patient areas, yet there is often a rapid throughput of patients with very disparate diagnoses. In addition, 6.4% of errors have occurred in the ICU setting where there will be one-to-one nursing in most instances.

Figure 20
Site of transfusion (n=343)

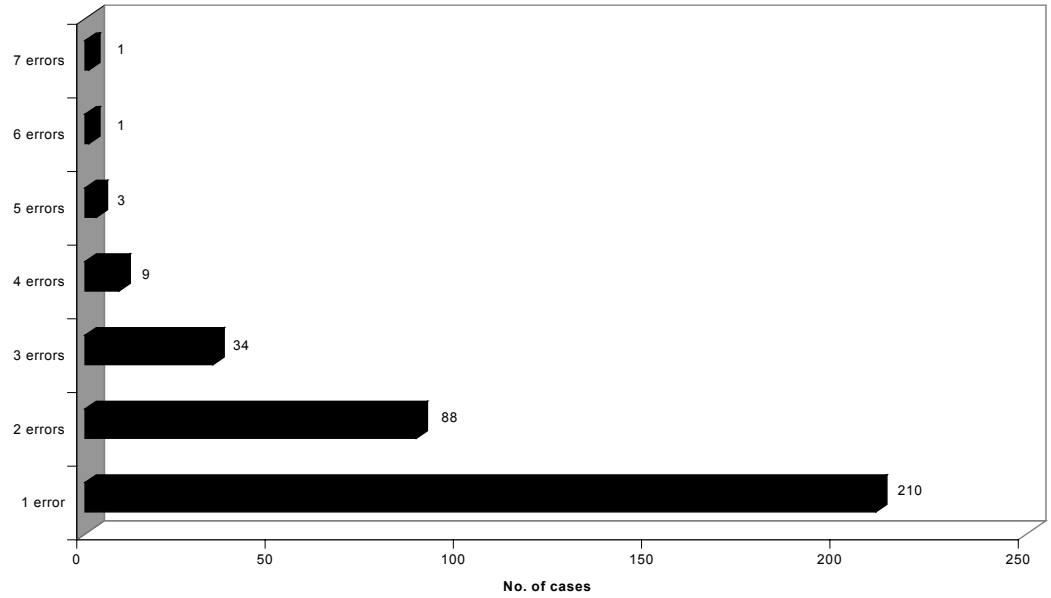


*** Other = 1 x Endoscopy Unit, 1 x Ambulance, 1 x Transfer between hospitals**

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

The SHOT scheme has consistently demonstrated that multiple errors have been implicated in many "wrong blood" incidents. In this 15 month reporting period multiple errors were noted in 137 (40%) of cases, with a total of 552 errors in the 346 fully analysed cases. In 14 cases there were four or more errors in the transfusion process. In the cases of multiple errors, most have included a failure of bedside checking which could have revealed a mistake arising earlier in the process. Of 103 bedside check failures, there were 39 instances where the wrong component had been collected and 46 instances where it was considered that another mistake earlier in the chain should have been noticed by the bedside check but this opportunity was missed.

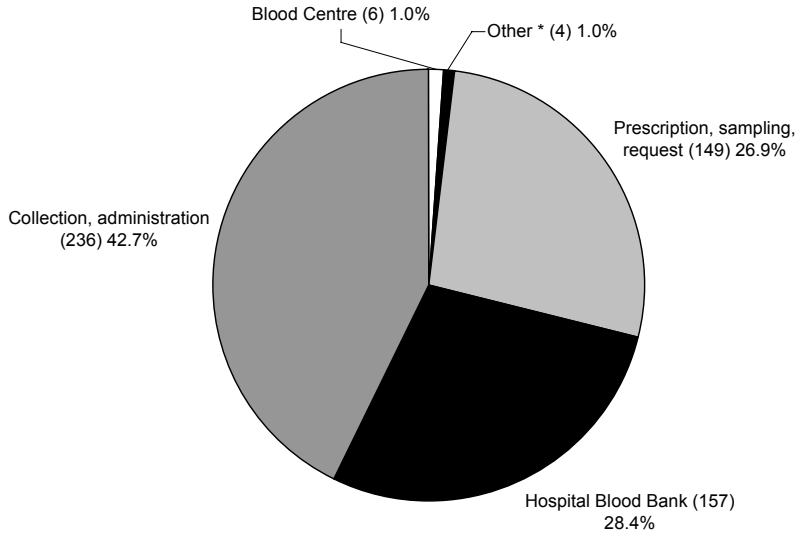
Figure 21
Total number of errors per case (total cases = 346; total errors = 552



Distribution of errors

The following pie chart (figure 22) shows the distribution, according to the main reporting categories, of a total of 552 errors from the analysis of 346 completed reports. A more detailed analysis of the distribution of total errors can be seen in table 19.

Figure 22
Distribution of total errors according to the main reporting categories (n=552)



***Other** = 1 x Incorrect Hb result – unable to determine cause
3 x Failure of Blood Bank refrigerator

Table 19
Distribution of procedural failures in terms of total errors (n=552 errors, 346 cases)

	Number of errors
Prescription, sampling and request	
Sample taken from wrong patient	6
Details on request form incorrect	14
Details on sample incorrect	13
Prescription of inappropriate and / or incompatible component(s)	19
Inappropriate Request	83
Other	13
Unknown	1
Total	**149**
Hospital Blood Bank	
Transcription error	3
Failure to consult / heed historical record	23
Grouping error	30
Missed Antibody(ies): Screen error	5
Missed Antibody(ies) Identification error	2
Missed Incompatibility	2
Selection / Issue of inappropriate component	24
Labelling error	8
Failure to irradiate	9
Crossmatch error	2
Crossmatch wrong sample	5
Failure to follow protocol	11
Incorrect serological reasoning	3
Clerical error	7
Technical Error	7
Failure to clear satellite refrigerator	5
Failure to detect error by Blood Centre	1
Other	10
Total	**157**
Collection and Administration	
Collection of wrong component	39
Failure to detect error earlier in the chain	46
Failure of bedside checking procedure	103
Wristband missing or incorrect	4
Inappropriate component selected by clinician	6
General administration Error	2
Failure to follow protocol	24
Other	12
Total	**236**
Supplying blood centre	
Inappropriate component supplied	1
Incorrect serology results supplied	2
Other	3
Total	**6**
Other	
Failure of Blood Bank refrigerator and / or alarm system	3
Wrong Hb result – unknown reason	1
Total	**4**

Analysis of total errors shows that there has been a marked increase in the proportion of errors occurring at the time of prescription, sampling and request (27% c.f. around 15% previously) with a proportionate reduction in errors occurring at collection and administration (43% - c.f around 50-55% in previous years). This may be due to the introduction of formal procedures for checking against patient identity at the time of collection of blood from storage sites combined with education. Possible alternative explanations are more complete reporting of errors occurring earlier in the transfusion process or a deterioration of practice at the request and sampling stage. The bulk of the increase in errors at the request stage has been in the number of inappropriate requests and it is notable that 60/83 inappropriate requests were failure to request irradiated components.

Multiple errors – how and when do they occur?

The following analysis of 552 errors occurring in 346 cases illustrates how some mistakes occur and the potential for multiple errors within a complex system requiring multiple human interventions. In many cases an error early in the chain should have been picked up but was not.

Errors in prescription, requesting of blood components and patient sampling

This year 26.9% of errors (149/552) in 39% of case reports (134/346) originated at the prescription, request, sampling stage.

Case 1

Labelling errors leading to failure to locate previous records

A 37 year old female patient required transfusion for anaemia due to end-stage renal failure. The dates of birth on the sample and request form were both incorrect. Two units of O RhD positive, Cytomegalovirus (CMV)-positive blood were issued but during transfusion of the second unit the patient noticed the discrepancy on the pack label and the transfusion was stopped. Provision of the correct details revealed that the patient had a previously identified anti-e (not found on the recent sample) and also that she required CMV-negative units. Both transfused units were found to be e-positive.

A number of similar cases were reported in which the correct patient received the intended unit but it was noted that staff had not picked up (or possibly had accepted) a discrepancy in the patient's identification details. While these are examples of "right blood in right patient" and caused no adverse event, the potential for serious reactions is evident from Case 1, above. Staff must not proceed with transfusion if any discrepancy in identification is noted. If these cases represent failure of the bedside check in that the discrepancy was not picked up then, clearly, there is the possibility that the wrong unit of blood may be given to a patient with similar details. These cases also represent failure of the blood transfusion laboratory 'look-up' system, which should enable previously known patients to be found even if there are discrepancies in identification details.

Case 2

Errors at all stages of the transfusion process

A 38 year old woman underwent removal of retained products of conception after spontaneous miscarriage. A pretransfusion sample was labelled with the wrong date of birth and this error was repeated on the request form. No hospital number was given. The blood group was O RhD positive and an antibody screen performed by IAT and enzyme techniques was wrongly interpreted as negative. Two units of blood were crossmatched – the low ionic-strength saline (LISS)-IAT match was also interpreted as negative. The hospital policy was to give women of childbearing age K-negative blood but this was not followed in this case. Two nurses checked the blood in theatre and administered the first unit without noting the date of birth discrepancy. Nursing staff on the ward noted the date of birth discrepancy when they came to hang the second unit and contacted the laboratory. A fresh sample was sent and was shown to contain anti-K. Repeat testing showed this was also present in the first sample. The first unit which had been transfused was then shown to be K-positive. The patient experienced no morbidity from this series of errors.

Failure to request the appropriate component (83 cases)

In 83 cases there was failure to meet the special requirements of the patient for irradiated blood, CMV-negative blood, special phenotype selection or provision of blood suitable for neonatal use. The most common error was

failure of medical staff to request irradiated components for patients at risk as defined in BCSH guidelines[7] (60 cases). In addition, two patients who required CMV-negative components received untested or CMV-positive blood. Eighteen patients were reported to have received fludarabine although actual numbers of fludarabine recipients may be higher as suggested by the underlying diagnosis in 10 cases (Non-Hodgkin's lymphoma (NHL), Acute Myeloid lymphoma (AML) etc).

In 12 cases errors in the provision of irradiated or CMV-negative blood arose at least in part because of failure of the haematology or transplant unit to communicate the patient's special needs to the laboratory in the hospital sharing the patient's care or to other departments in the hospital to which the patient had been temporarily transferred (e.g. ICU, renal). None of these incidents led to serious morbidity or mortality but there was potential for the development of fatal GVHD or CMV infection.

Case 3

Communication failures relating to autologous units

A 30 year old bone marrow donor had predonated 2 units of autologous blood to cover his bone marrow harvest. These had been received in the hospital transfusion laboratory before the harvest. The request form for blood for the donor did not state that he had autologous blood available, and unirradiated, allogeneic units were transfused during the bone marrow harvest, with the potential risk of inducing graft-versus-host disease in the transplant recipient. There seems to have been no system in place to allocate the donated units to the donor's hospital transfusion laboratory record before a sample and request form were received from the ward. Communication from the doctor who sent the sample and made the request was inadequate, as was the blood transfusion laboratory record keeping facility.

Case 4

Over-reliance on hospital numbers may cause errors

A 65 year old patient with NHL (?given fludarabine) was admitted as an emergency through A&E and transfused with unirradiated blood. The laboratory had not identified that he had a transfusion record which stated that he required irradiated blood, as he was registered in the system under a hospital number from the Cancer Centre rather than the hospital number he was given on admission. There have been several cases reported where patients who already have a transfusion record stating that they had antibodies or special requirements have not been identified because a different hospital number has been used. IT systems should be capable of searching on the basis of name and date of birth, and should highlight matches which only differ in the hospital number. Laboratory staff need to be capable of undertaking adequate patient searches.

Communication Failures in Shared Care

In 20 patients errors arose because of failure of tertiary referral centres to communicate special requirements to other hospitals or units sharing the patients care. These included:-

- failure to advise of planned stem cell harvest or bone marrow harvest, leading to transfusion of unirradiated components in the few days prior to collection. In one case the bone marrow harvest was discarded and in another a child's stem cell collection was abandoned, after a central line had been inserted to allow this to take place.
- failure to advise of donor/recipient ABO group differences leading to administration of incompatible components.
- failure to provide irradiated components to transplant recipients who had been transferred for renal support or who were re-admitted through A&E.
- elective admission for surgery at a private hospital where the past history of autologous stem cell transplant was not elicited.
- failure to irradiate blood for a neonate who had received intrauterine transfusions at a fetal medicine unit. The obstetricians attending the delivery were apparently unaware of this fact and the maternal details on the hospital transfusion laboratory computer could not be linked to the record of an as yet unborn patient.

Hospital Transfusion Laboratory Errors

There were a total of 157 errors in this category occurring in 120 case reports.

This year in 35% of cases (120/346) the first error occurred in the hospital transfusion laboratory. In many cases errors made within the laboratory cannot be detected further down the transfusion chain, although in some cases involving 'special requirements' they should be noticed by the nurse commencing transfusion.
Of the 157 laboratory errors, 88 occurred during routine working hours and involved 84 state registered BMSs, 1 supervised medical laboratory assistant (MLA), 2 locum/agency staff and 1 trainee. The 49 errors made out of hours involved 16 BMSs who worked regularly in the blood bank and 33 who did not. In 16 other cases involving 20 errors the grade of staff was not stated. This information is summarised in figure 23. Table 20 gives more detail about the errors and grades of staff involved.
31.2% of laboratory errors occurred outside normal working hours. As stated in last year's report it is not possible to comment on the significance of this information in the absence of relevant denominator data but it is hoped that some indicative data can be collected over the next year. Staff in hospital laboratories who can readily break down their workload into "normal working hours" and "outside normal working hours" are encouraged to make these data available to the SHOT office when reporting errors or near-miss events. Further work is required to provide relevant denominator data.

Figure 23
Staff involved in laboratory errors (n=157)

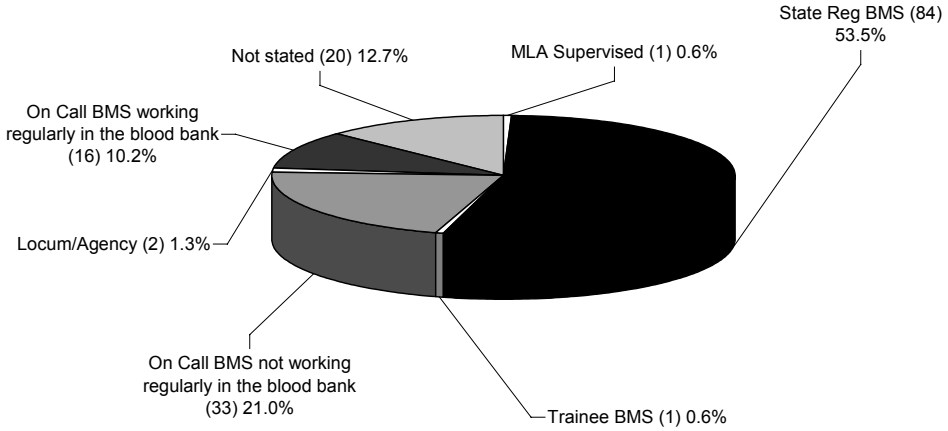


Table 20
Laboratory errors and grade of staff involved (n=157)

Error	Total number of errors	State registered BMS, routine, regularly working in blood bank	State registered BMS, on call, regularly in blood bank	State registered BMS, on call, not regularly in blood bank	Other staff	Unstated
Sample transposition	**5**	1	2	2	0	0
Failure to consult / heed historical record	**23**	14	1	6	1	1
Incorrect group	**30**	13	8	5	0	4
Missed antibody(ies)	**7**	2	1	2	0	2
Missed incompatibility / crossmatch error	**4**	0	0	2	0	2
Incorrect labelling of component	**8**	6	0	2	0	0
Selection / issue of inappropriate component	**24**	12	1	6	2	3
Failure to clear satellite refrigerator	**5**	5	0	0	0	0
Failure to irradiate	**9**	6	0	2	0	1
Clerical error	**10**	8	1	0	0	1
Other procedural error	**22**	11	0	6	0	5
Other	**10**	6	2	0	0	2
Total	**157**	**84**	**16**	**33**	**3**	**21**

The largest single areas of laboratory error are in “failure to consult/heed historical record”, “incorrect group” and “selection and issue of an inappropriate component”. As can be seen from the table above, these errors are, in the main, being made by trained staff working routinely in the blood bank, rather than by on-call staff.

Failure to consult/heed historical record (23)

In 23 cases laboratory staff failed to note or act on a previous record which would have highlighted the previous presence of an alloantibody, for example, or special requirements in component selection. This included 10 cases where the need for irradiated components was already recorded on the hospital transfusion laboratory database yet this was missed or not acted on.

Case 5

Date of birth discrepancy leads to failure to identify recent antibody record

An 81 year old woman required routine transfusion because of gastrointestinal bleeding. A pre-transfusion sample revealed the presence of a weak anti-K and K-negative units were issued. Three days later a further sample was received with a request for 3 units. The date of birth on this sample differed from the earlier one by one day. The historical record was therefore not identified and as no antibody was detected in the sample, the units were not K-typed, however they appeared compatible. The error was revealed following a further request 12 hours later. Fortunately the transfused units were subsequently shown to be K-negative and no adverse event occurred. The date of birth on the second sample was, in fact, correct. It is not known if the patient’s hospital number was used to search the database nor whether the IT system would have restricted the “view” of patient details, after registration, only to that which was an identical match, or if “near misses” (on date of birth, for example) would have been shown on the screen.

Grouping errors (30)

There were 30 errors in blood grouping, including 16 cases in which the wrong RhD group was obtained and 14 errors in ABO grouping. Seven of the RhD group errors resulted in errors in anti-D administration. However in

all cases in which RhD incompatible components were given as a result of a laboratory grouping error, the recipients were male. Four ABO grouping errors led to incompatible transfusions, in which one patient died of unrelated causes whilst the other 3 survived without ill-effects.
17/30 grouping errors (57%) related to rapid group techniques; 12/17 were outside normal working hours and 14/17 were in emergency situations. Sixteen of these errors were detected when retrospective routine grouping was carried out.

Case 6

Illogical "resolution" of anomalous results – failure to spot an obvious error

A 52 year old male with anaemia due to lymphoma required an elective transfusion of four units of blood. Blood grouping was performed using microplate techniques by the state registered blood bank BMS and this was interpreted as being anomalous as there was a reaction with Anti-A, Anti-B, A_1 cells and both anti-Ds. The BMS decided to repeat the group before selecting the red cell units. The wrong sample appears to have been selected and this grouped as O RhD positive. Four units of Group O RhD positive red cells were cross-matched and administered. The sample selection error was revealed the following day when routine grouping showed that the initial reaction pattern had been correct – the patient was Group A_2B RhD positive with anti-A_1. As the transfusion was compatible no adverse reaction occurred.

Selection/issue of inappropriate component (24)

There were 6 cases in which expired blood was given to patients, at least in part because units were issued towards the end of their shelf-life. It is difficult in these cases to know whether this was intentional on the part of the laboratory in anticipation that they would be used within a few hours of issue. Incompatible platelets, FFP and cryoprecipitate were issued in 5 cases, with no morbidity other than serological discrepancies and the possibility of RhD sensitisation in one female baby. Errors in the selection of components for infants were seen in 4 cases, including failure to select pathogen-inactivated FFP.

Labelling of blood components (8)

Labelling errors, in which the details of one patient were applied to a pack intended for another patient, will generally result in 2 mislabelled components with the potential for harm to two patients. In one case (see Case 23, below) this led to significant morbidity.

Errors in the collection and administration of blood components

There were 236 errors in this category occurring in 159 case reports comprising 42.7% of all errors.
As in previous years this remains the most frequent point of error, although it is proportionately smaller than in any previous year.

Collection of incorrect component (39)

Table 21
Collection errors according to grade of staff involved and whether or not a formal check was made at this stage

GRADE OF STAFF	FORMAL ID CHECK		
	Yes	**No**	**Unstated**
Registered Nurse	8	4	1
Unregistered Nurse	3	1	0
Porter	3	7	0
Theatre Staff	0	2	0
Unknown	0	3	4
Other [1]	0	3	0

[1] 1 x clinical support worker, 2 x doctor

In most cases where the grade of staff is known, the individual collecting the blood has been a nurse and a formal identity check has apparently been carried out at the time of collection, yet the wrong unit has been collected. Portering staff appear to be less likely to have carried out an identity check, perhaps reflecting a failure of hospital policy and lack of appropriate training of portering staff.

Failure of bedside checking procedure (103)

Failure of bedside checking occurred in 30% of all IBCT cases. It is disappointing that this is still the commonest site of error, despite emphasis on the need to address this in all previous SHOT reports. In most cases where this has gone wrong there has been no identification of the patient at the time of administration and in 39 cases there has been a failure to pick up previous collection errors. There were only 4 reported cases of missing wristbands although this is a difficult point to determine accurately some time after the event.

Table 22
Outcome of bedside errors (103)

Category	Survived/ no ill effects	Major morbidity	Died unrelated to tx.	Died possibly related to tx.	Died probably related to tx.	Died definitely related to tx.	Unknown	Total
Major ABO incompatibility	10	2 [1]	2	1	0	0	0	**15**
RhD incompatible	2	0	0	0	0	0	0	**2**
ABO / RhD compatible	51	0	2	0	0	0	2	**55**
Other red cell incompatibility	3	0	0	0	0	0	0	**3**
Special requirements not met	6	0	4	0	0	0	1	**11**
Inappropriate transfusion	4	1	0	0	0	0	0	**5**
Anti-D	10	0	0	0	0	0	0	**10**
Other [2]	2	0	0	0	0	0	0	**2**
Total	**88**	**3**	**8**	**1**	**0**	**0**	**3**	**103**

[1] Recovered from intravascular haemolysis
[2] 1 expired unit given, 1 transfused more than 72hrs post cross-match

Table 23
Grades of staff involved in bedside incidents (n=103)

Grade of Staff	Number of cases
Registered nurse & registered nurse	53
Registered nurse and unregistered nurse	3
Registered nurse & doctor	5
Registered nurse & medical student	1
Registered nurse and unknown	3
Registered nurse only	15
Registered nurse & other [1]	2
Doctor & doctor	2
Doctor & other [2]	1
Doctor only	10
Other only [3]	4
Unstated	4

[1] 1 x auxiliary, 1 x student nurse
[2] 1 x Operating department practitioner (ODP)
[3] 1 x ODP, 3 x midwife

Bedside errors led to 15 cases of administration of ABO-incompatible blood, resulting in severe morbidity in 2 cases and one possibly related death, while two further patients died unrelated to the transfusion. The remaining 10 patients survived without any ill-effects.

In 70 cases two individuals were responsible for the bedside check, with one person responsible in 29 cases. Nurses were involved in 82 cases but as the bulk of transfusions are administered by nursing staff no conclusion can be drawn from this other than that the "safe transfusion" message has so far failed to reach both nursing and medical staff. Patients have received the wrong blood even though a bedside check has apparently been carried out. Observational studies (Effective use of Blood Group, Scottish National Blood Transfusion Service, unpublished data) have shown that in many cases the documentation has been checked against the details on the blood pack but staff have failed to check the identity of the patient, either verbally or using the wristband.

Inappropriate component selected by the clinician (6 cases)

These included the selection of the wrong group of FFP or the wrong unit of platelets, in situations where nursing or medical staff were given the responsibility of accessing FFP or platelet stocks out-of hours, and included the inappropriate use for neonates of blood provided for the mother, or emergency "flying squad" blood. These cases illustrated poor communication with the hospital transfusion laboratory over anticipated requirements for babies affected by haemolytic disease of the newborn and also a lack of serological knowledge (which is not particularly unexpected) amongst paediatric or obstetric staff.

Case 7

Lack of understanding of significance of maternal antibody in relation to blood selection

An antenatal patient with known anti-c was admitted for induction of labour shortly after an ultrasound scan which had shown a healthy fetus. The paediatricians had contacted the hospital blood bank the day before delivery and were advised that suitable blood for exchange transfusion would be requested from the blood service. At induction the fetus showed severe distress resulting in an emergency caesarean section. The infant was hydropic with a Hb of 60/L. The paediatrician gave an urgent top-up transfusion (50mL) using "flying squad" blood. Several hours later they requested blood for an exchange transfusion and notified the laboratory that "flying squad" blood had been used. The paediatricians appeared to have been unaware that the blood used would have homozygous expression of the implicated antigen (Group O rr – i.e. c-positive). The infant appeared to have experienced no adverse reaction although any increased haemolysis is likely to have been managed by the subsequent exchange transfusion. The hospital has changed its procedure for management of similar cases, requesting earlier notification of intended delivery and the provision of compatible Group O blood for the mother in order that this can also be used for an immediate top-up in the neonate in an emergency.

Cases 8 and 9

Wrong blood to baby – 2 cases in one unit reveal failure to "close the loop"

A preterm infant required a routine top-up transfusion for anaemia, during normal working hours. Pretransfusion testing and cross-matching was performed and a labelled unit was placed in the blood bank refrigerator. A porter collected one unit of O RhD negative "flying squad" blood from the refrigerator instead of the cross-matched unit, with no identity check and without signing the register. Two qualified nurses apparently "checked" the unit prior to administration, even though the pack label and issue report showed clearly that this was "Emergency O Negative".
Three weeks later the same scenario was repeated with a second baby on the same unit! The staff have identified that although appropriate policies were "in order" there were evident training issues to be addressed.

Inappropriate transfusion episodes

Currently SHOT does not record a category where patients received components which they did not require (other than in cases where a patient received blood intended for someone else). However, these instances are relatively common – either inappropriate administration due to lack of knowledge of the appropriate guidelines or due to spurious laboratory results as described below.

Inappropriate transfusion due to spurious results on FBC or coagulation screen

In 21 cases, patients received red cells (19), platelets (1) or FFP (1) as a result of errors in sampling, testing or communication of haematology results. In the 19 patients who received red cells which were not, in fact, required, the problem seems to have arisen during sampling in 10 cases – for example due to drawing blood from the drip arm or perhaps due to allowing blood to settle in a syringe before filling the sample tubes. In four cases verbal transmission of results to the ward, or between different staff on the ward has led to the wrong Hb being recorded. In 2 cases Hb results from gas analysers were assumed to be accurate and the patient transfused on this basis. One patient who received FFP unnecessarily seems to have had a spurious coagulopathy generated by sampling from the arm which was the infusion site for a red cell transfusion as the group on the coagulation sample differed from the pre-transfusion sample drawn slightly earlier. One patient received platelets when thrombocytopenia was diagnosed on a sample containing clots. The discrepancy between the spurious Hb levels and the patient's actual Hb was up to 70g/L in some patients, yet the results appear to have been accepted as in keeping with the clinical picture by the medical staff prescribing the blood. In two patients (see Cases 16 and 17, below) the inappropriate transfusions are felt to have contributed to the patients' deaths.

Case 10

Iatrogenic polycythaemia

A haematologist was asked to advise on a patient with post-operative polycythaemia. This 85 year old female had been admitted with gastrointestinal bleeding and received a 4 unit red cell transfusion as ward staff had reported the Hb to be 91g/L. In fact the correct result was 145g/L. The cause of the polycythaemia became clear when the laboratory results and transfusion history were compared!

Cases 11 and 12

Don't rely on Hb levels from blood gas analysers

Two patients were transfused on the basis of Hb results of 50g/L from blood gas analysers. A sample from one of the two was later checked in the laboratory and found to have a Hb of 117g/L pre-transfusion. The second patient had an Hb of 157g/L after the transfusion of 5 units of red cells. It is estimated that the pre-transfusion Hb was, in fact, around 100g/L.

Case 13

Unauthorised access to blood bank refrigerator

A junior doctor was observed drawing blood from a pack in the blood bank refrigerator. He advised that he was conducting a "potassium level audit" and that he had been carrying this out for the previous three days. The BMS discovered that nine packs in the refrigerator had been similarly punctured and one sampled unit had already been transfused. The doctor was ignorant of the potential risk of bacterial contamination of the punctured units. This potentially disastrous incident highlights a number of issues including the need for adequate supervision and training of junior medical staff and for restriction of access to blood storage areas.

Errors originating at the supplying blood centre

There were 6 errors in this category occurring in 6 case reports

Case 14

Failure to irradiate granulocytes – particular risks of infrequently used components

A 34 year old male patient with acute lymphoblastic leukaemia received three units of granulocytes from a Blood Service donor. The units were not irradiated and were not CMV-negative. On arrival at the hospital blood bank they were issued by the on-call BMS who was not regularly working in the blood bank and administered to the patient. No adverse consequences were identified. All granulocyte transfusions MUST be irradiated and, because of their high white cell content, carry a significant risk of CMV transmission to susceptible patients. This is an infrequently used component and it is not surprising that an on-call BMS would not be aware of the necessity to irradiate this product.

Errors in anti-D administration

SHOT does not seek to record errors in anti-D administration (either of omission or commission) due to failure to follow guidelines. However errors due to laboratory grouping errors, patient misidentification or wrong serological reasoning are included. There were 43 reports involving anti-D administration – 8 cases in which anti-D was indicated but either not given or given in an inadequate dose. In one of these cases the BMS issued Hepatitis B immunoglobulin, in error. In 35 cases patients received anti-D which they did not require. In 4 cases the patient was known to have immune anti-D present, 4 patients had delivered RhD negative babies, one case involved anti-D cover for administration of platelets which were, in fact, from a RhD negative donor while in all other cases anti-D was administered to patients who were RhD positive. In most instances this was due to midwives administering anti-D to patients before grouping results were available or to patients who had already been shown to be RhD positive. Routine antenatal prophylaxis was given to three RhD positive patients by the same midwife working in a GP's practice – it was not clear if this simply reflected lack of training/understanding of the antenatal prophylaxis programme. In 8 cases anti-D was administered to the wrong patient because of misidentity of the patient at the time of administration or telephone communication of incorrect results by the laboratory.

Case 15

A series of failures leads to repeated unnecessary administration of anti-D

An antenatal patient underwent routine blood grouping by community midwife. The result, A RhD positive, was written on the patient-held records. Inexplicably, the midwife then wrote "information given re Rh Neg" and made an appointment for routine anti-D prophylaxis. The transfusion laboratory issued anti-D without checking their records for the blood group. Anti-D was administered by the midwife, again without checking records. A further appointment was made for 34 weeks gestation and the same scenario was repeated other than that blood group A pos, appeared on the issue form, but was not noted. Anti-D was given by the same midwife. At delivery, the patient enquired about anti-D at which point previous errors were noted. A number of changes have been implemented in order to reduce the risk of recurrence.

Outcomes

Of the 346 fully analysed cases there were 32 cases of major ABO incompatibility, including 2 cases which were also RhD incompatible and 1 case who also failed to receive irradiated components. There were 19 cases of RhD incompatibility (of which 13/19 errors originated in the laboratory), 18 cases where other red cell antigen incompatible transfusions were given, and 106 incidents which resulted in ABO and RhD compatible transfusions.

The remaining cases comprised 83 cases of failure to provide for special requirements (including 69 non-irradiated, 1 neither irradiated nor CMV negative and 2 not CMV negative), 43 cases of errors in anti-D immunoglobulin administration, 31 cases of an inappropriate or wrong component transfused, and 14 "other". (including administration of expired units, transfusion later than 72 hrs post-crossmatch, incorrect storage during transfer of patient, freezing of red cell units due to incorrect packaging).
There were 3 deaths which may have been related to the adverse event.

Mortality due to the adverse events

Case 16

A spurious Hb result which may have contributed to this fatal outcome

This 92 year old woman was admitted with a gastrointestinal haemorrhage and cerebrovascular accident. A sample drawn from the drip arm gave an Hb result of 81g/L and a transfusion of 4 units of red cells was given. The Hb post-transfusion was 176g/L suggesting that that the pre-transfusion Hb result was spurious. The patient developed cardiac problems and died shortly afterwards. It was felt that the unnecessary transfusion may have contributed to her death.

Case 17

Inappropriate transfusion contributing to death of a patient

A 96 year old woman was admitted with a gastrointestinal haemorrhage. A full blood count sample sent to the laboratory was underfilled and gave an Hb result of 50g/L. The result was phoned to the ward with a request to repeat the test as soon as possible. The result was authorised in the computer with a text comment "sample underfilled, result subject to error". No repeat sample was sent but a 6 unit cross-match was ordered. Further samples were requested by the hospital transfusion laboratory as the group and screen sample was also small. Three units were transfused and a post-transfusion Hb was 200g/L. The patient developed circulatory overload and an emergency venesection was requested. The patient died the following day. The pre-transfusion Hb was, in fact, 170g/L. The ward computer access to the patient's results did not display text comments.

Case 18

Failure of bedside check leading to intravascular haemolysis

A 67 year old woman was terminally ill due to bronchiectasis and had a history of poorly controlled diabetes. She was not intended to receive a transfusion and no pre-transfusion sample had been sent. One unit of Group A RhD positive blood which had been matched for another patient was administered to this patient who was Group O RhD negative. She developed loin pain and became jaundiced, with an elevated alanine aminotransferase. Following this the patient elected to receive no further treatment and died 5 days after the event. Although the patient was already terminally ill at the time of the error it was felt that this hastened her demise.

Case 19

Dangers of incompatible plasma infusions (1)

A 21 year old man with a haematological malignancy who was Group B received 4 units of incompatible Group O FFP. The FFP had been selected from the freezer out-of-hours by a Nurse Practitioner in a hospital where there was no on-call transfusion service. The patient developed hypotension and haemoglobinuria and subsequently went on to develop hepatorenal failure, leading to death. It is not clear how much of this was due to the transfusion reaction or to progression of his malignancy. This hospital is considering issuing only AB FFP out-of-hours in future and an on-call transfusion service is to be introduced.

Major morbidity

Four patients who received ABO incompatible transfusions experienced major morbidity and one female patient who received a RhD incompatible transfusion developed anti-D which is likely to affect future pregnancies. Two further female patients who received RhD incompatible components were of potentially child-bearing age. Case 25, below, is recorded as dying of unrelated causes but clearly suffered major morbidity due to the transfusion error before her demise.

Case 20

Blood collection error leading to ABO incompatibility

A 58 year-old man, Group O RhD positive, who had undergone transurethral resection of bladder tumour received approximately 200mL of Group A RhD positive blood. He experienced rigors, hypotension and subsequently developed renal failure. The incorrect unit had been collected from a satellite refrigerator by a qualified nurse and a single qualified nurse had checked and set up the transfusion. The patient made a good recovery after being transferred to a high-dependency unit.

Case 21

Dangers of incompatible plasma infusions

A 7 year-old boy with leukaemia who was Group B received a transfusion of pooled platelets which were Group O and which had not been shown to have low titres of anti-B. He became anaemic and jaundiced, with a positive DAT and an incompatible cross-match against Group B red cells. He required in-patient admission and a red cell transfusion.

Case 22

Laboratory labelling error and failure of bedside check result in ABO-incompatible red cell transfusion

A 30 year old man with gastrointestinal bleeding became febrile, developed rigors, back pain and bronchospasm and became hypotensive within the first 50mL of a red cell transfusion. The patient was Group O and the pack, which was labelled with his details, was Group A. A second wrongly labelled unit was returned to the laboratory which noticed the error and immediately contacted the ward, but the transfusion had already been commenced. The error in the labelling was not identified by the two nurses who carried out the bedside check. The patient recovered from the effects of intravascular haemolysis.

Case 23

Discrepant RhD-typing leading to RhD-immunisation

A 23 year old woman was transfused during an acute attack of porphyria. She had been previously grouped as O RhD negative but on more recent re-grouping using an automated Diamed system she grouped unequivocally as O RhD positive on 2 occasions. It was assumed that she had a weak D and she subsequently received 2 units of Group O RhD positive blood. She developed anti-D and had a positive Direct Antiglobulin Test months later. It is possible that this patient has a Partial D phenotype but no subtyping had been carried out at the time of submission of the report.

Case 24

Failure to manage a detected error effectively leads to mismatched transfusion

This teenage girl was admitted with major trauma due to a road traffic accident and was being resuscitated in the Accident and Emergency Unit. Units of blood for another patient (different name, DOB and hospital number) were collected by an anaesthetist from the blood bank refrigerator but this error had been noted by the nurses performing the bedside check. The units were placed on a bench away from the bedside but in the same resuscitation room and one was subsequently picked up and administered by another doctor without further checking. This group O RhD positive patient received over 100 mL of group B RhD positive red cells. She developed acute intravascular haemolysis and severe anaemia (Hb 25g/l) though the anaemia was at least in part due to her injuries from which she subsequently died.

The outcome of all IBCT cases is summarised in Table 24

Table 24

Outcome of cases of incorrect blood component transfused (n=346)

Category	Survived / no ill effects	Major morbidity	Died unrelated to tx.	Died possibly related to tx.	Died probably related to tx.	Died definitely related to tx.	Outcome unknown	TOTAL
Major ABO incompatibility[1]	23	4[2]	3	2	0	0	0	**32**
RhD incompatible	18	1[3]	0	0	0	0	0	**19**
ABO/RhD compatible	97	0	5	1	0	0	3	**106**
Other red cell incompatibility	15	1	2	0	0	0	0	**18**
Inappropriate transfusion	27	2	1	0	1	0	0	**31**
Special requirements not met [4]	73	1	7	0	0	0	2	**83**
Anti-D	43	0	0	0	0	0	0	**43**
Other	14	0	0	0	0	0	0	**14**
Total	**310**	**9**	**18**	**3**	**1**	**0**	**5**	**346**

1 Includes 2 case which was also RhD incompatible
2 Includes recovered from intravascular haemolysis
3 RhD sensitisation in female of child bearing potential
4 Irradiation/CMV negative/phenotype selection/ blood suitable for a neonate etc.

Procedural review

Table 25
Hospital Transfusion Committees

Number of responses	Response
8	No response
230	No, but will be discussed at a future meeting
107	Yes
1	No Transfusion Committee in place

Table 26
Summary of changes made to policies / procedures (n=194)

Number of changes	Summary of change
88	Changes to or new documentation, techniques, policies, procedures, etc.
24	New or additional training
26	Review of existing policies / procedures / protocols
6	Upgrade, renewal, or acquisition of equipment, including computer
16	Reiteration of existing policies / procedures / protocols
7	Introduction of new policies / procedures / protocols
2	Meeting pending – problem to be discussed
6	New or amended software introduced now or later
2	Patients carry cards
6	Developing a system of communication / liaison for shared care patients
2	Audit of existing procedures
2	Considering introduction of bar coding
6	Considering acquiring new or additional resources (including staff)
1	Unspecified

Table 27
Summary of comments made by reporters who said that no changes had been made or who did not respond to the question (n=52)

Number of comments	Summary of comments
23	Current policies / procedures / protocols reiterated
9	Case has been or will be reviewed internally
3	Proposal forwarded to Trust
2	Staff removed from rota
1	Counselling of staff
6	Policies / procedures / protocols under review
1	Risk assessment underway
4	Corrective action to be taken later
3	Staff re-trained

COMMENTARY

- For the sixth consecutive year, even after taking into account the change in the reporting period, transfusion errors remain by far the commonest serious adverse event reported to SHOT (71.7%) and the trend shows no signs of a plateau. It is encouraging that staff are demonstrating increasing awareness of, and confidence in, the SHOT scheme. This is may be the cause of the continued steep rise in reporting, rather than that more errors are being made.

- There remains evidence of weakness at all stages of the transfusion process, particularly at the time of collection of blood from storage sites and bedside checking, the latter being the commonest site for errors (103/552, 18.7%). Good practice guidelines covering these aspects of transfusion practice were published in 1999[6] but have not been widely implemented into practice. The guidelines are currently under review. 'Bedside' checking may frequently take place away from the bedside and focus on the paperwork, losing sight of the main purpose which is to check that the right blood is being given to the right patient. In most reported errors two members of staff have been involved in the bedside check, - denominator data is required to establish whether checking by a single or 2 person(s) is more reliable. Positive identification of patients is a major safety issue with potential impact not only on blood transfusion but also on drug administration, dietary management, performance of diagnostic procedures and surgical interventions.

- Collection of the wrong unit from a theatre satellite refrigerator occurred in 39/346 (11.3%) cases and administration was not prevented by the bedside check. Theatre patients may have their name bands removed to allow vascular access, and early signs of a transfusion reaction may be obscured by the unconscious state. A surgical patient who requires blood may be considered to have other reasons for developing a tachycardia or hypotension and a transfusion error may not be suspected until one or more units have been transfused.

- Almost a third of all errors (157/552, 28.4%) continue to occur in hospital transfusion laboratories and, as yet, there has been no major initiative to address this. In many cases BCSH guidelines on pre-transfusion testing[13] have not been adhered to, and the underlying reasons for this need to be identified.

- Shared care arrangements, particularly for patients with malignancies who have undergone stem cell transplants, fail repeatedly, with lack of communication of special transfusion requirements to other hospitals or even to other departments within the same hospital. Haematology medical staff have apparently been unaware of guidelines on irradiation of blood components[7] and improved induction and education is needed. Failure to irradiate components for recipients of fludarabine, particularly oral preparations, has occurred in at least 18 cases. In the 60 failures to request irradiated components there has been no mention that the patient carried a card indicating this requirement or that the hospital pharmacy was involved in local protocols.

- There is only limited evidence that errors are being fully investigated and seen as learning opportunities. This raises concerns about how transfusion errors are being managed within hospitals.

- Anti-D administration errors comprised 43/346 (12.4%) of all reports, the most common scenario being administration of anti-D to RhD positive recipients. It is not clear to what degree this is a training issue.

RECOMMENDATIONS

- **Continued reporting of transfusion errors to SHOT is essential, as directed by HSC 2002/009[2] and in the earlier HSC 1998/224[1]. All hospitals, and all departments within hospitals should participate in the scheme and SHOT recommendations should be considered by hospital Clinical Governance Committees to determine what local action needs to be taken.**

- **In order for patients and staff to derive full benefit from the SHOT scheme, local initiatives to disseminate the main messages of the SHOT report are essential. These could form part of induction sessions for all staff groups or be regular sessions at hospital "Grand Rounds" sessions or departmental training programmes.**

- **Reporting should be the norm and full investigation of reported incidents should be carried out by individuals who are familiar with good practice guidelines for transfusion. SHOT findings should be part of mandatory training for all staff involved in the transfusion process.**

- **All staff should be made aware through the Risk Management Committee of transfusion errors occurring in their department and in other departments within the hospital. This should not reveal the identities of individuals concerned, the emphasis being on avoiding repetition of errors and encouraging staff to analyse their working practices to identify potential "weak links" which can be remedied.**

- **Clear policies must be developed for communicating special transfusion needs of patients to other hospitals or units which may share their care. This is particularly relevant to stem cell transplant recipients. Active involvement of patients in this aspect of their care could reduce the frequency of these errors.**

- **Increasing use of fludarabine, particularly oral preparations, means that many more patients are susceptible to TA-GVHD. Pharmacy departments should play a role in notifying patients and hospital blood banks when this therapy is commenced. The forthcoming BCSH guidelines on the avoidance of Transfusion Associated GVHD (which extend the current guidelines for irradiation[7]) include advice on communication where there is shared care and include input from the Pharmacists/Pharmacologists community.**

- **Improved training of midwives in relation to anti-D administration is necessary. There is increasing risk of mis-administration with the rolling out of the routine antenatal prophylaxis programme. More secure and explicit communication of antenatal and postnatal results is required.**

- **Human error in relation to patient identification is still the commonest problem leading to wrong-blood-in-patient. Educational initiatives have been inadequate in resolving this problem. Patients should be empowered to be involved in the bedside checking procedure.**

- **Investment in the development and evaluation of technological solutions is essential if errors in the transfusion process are to be significantly reduced.**

11. NEAR MISS EVENTS

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

The concept of "near miss"

The concept of "near miss" events has been borrowed from air traffic control to denote an accident which came close to happening but did not, whether through luck or judgement. "Near miss" is a useful concept. In air traffic control a "near miss" usually describes an incident where two aircraft fly within a defined distance of each other which is close enough to cause alarm and concern but no accident or loss of life takes place. It can be applied to various clinical situations, but there is some confusion defining what constitutes a "near miss" in clinical practice. In the definition above for blood transfusion a "near miss" is an error that could have led to the wrong blood being given but did not.

Nashef[14] recently suggested a useful classification of "near miss" events in a letter to the Lancet. In the first type of situation described by Nashef an adverse event occurs, but a system is in place to detect and correct it which works as planned and so no harm is done. It is this type of "near miss" which we are describing in this chapter, and Nashef suggests that the majority of such events, though important, go unrecorded. In the second type of "near miss" an adverse event occurs and one or more of the systems in place fail to detect and correct the error, however, no harm is done, perhaps for unconnected reasons. This is analogous to IBCT reports in which the wrong blood is given but fortuitously is ABO compatible. The third type of "near miss" is that in which an adverse event occurs and one or more of the systems in place fail to detect or correct it and harm is sustained, but falls short of the worst possible outcome. If this scheme were to be adopted then many of the events currently recorded by SHOT as IBCT would be considered as 'near-misses', however there are no plans to change the current classification, as 'wrong blood' errors are no less serious when ABO compatibility saves the recipient from a potentially life-threatening outcome.

In order to obtain a full picture of errors and the causes of errors in blood transfusion, it is important to gather all "near miss" information, so that corrective action can be taken to prevent recurrence[15]. High quality data on "near misses" is needed to strengthen preventative efforts and to reduce the burden of transfusion related incidents on individuals and on the National Health Service. Lessons from the aviation industry have shown that improving collection of "near miss" data will at first increase the number of such events reported, but at the same time will lead to a reduction in the number of actual serious events, in this case air crashes with catastrophic consequences. To extrapolate to blood transfusion it may be that once effective systems are in place in all hospitals to detect and document "near miss" events in blood transfusion we might see a reduction in or perhaps a complete prevention of fatal occurrences of wrong blood to patient.

Participation rate

Participation in the SHOT "near miss" scheme is recommended in the Health Service Circular HSC 2002/009[2] but not yet mandated for Clinical Pathology Accrediation or CNST, and is essential within Trusts as part of their risk management and clinical governance strategies. Most hospitals now participate in SHOT reporting of actual adverse events, including instances where wrong or inappropriate blood components were transfused, regardless of whether the patient suffered any harm as a result. This year hospitals have been actively encouraged to submit "near miss" data as well.

This year 146 hospitals out of a total of 405 have reported "near misses" (36%), whilst 50% of participating hospitals state that they have experienced "near miss". Reporting is skewed as some hospitals are sending a large number of "near miss" reports whilst others are not sending any. This is likely to be an indication of differences in systems for identifying and documenting such events in different hospitals rather than a true difference in incidence. Therefore the data available are likely to be the 'tip of the iceberg' and may well reflect those "near misses" that were easy for the haematologists or BMSs to identify and deal with. This may explain

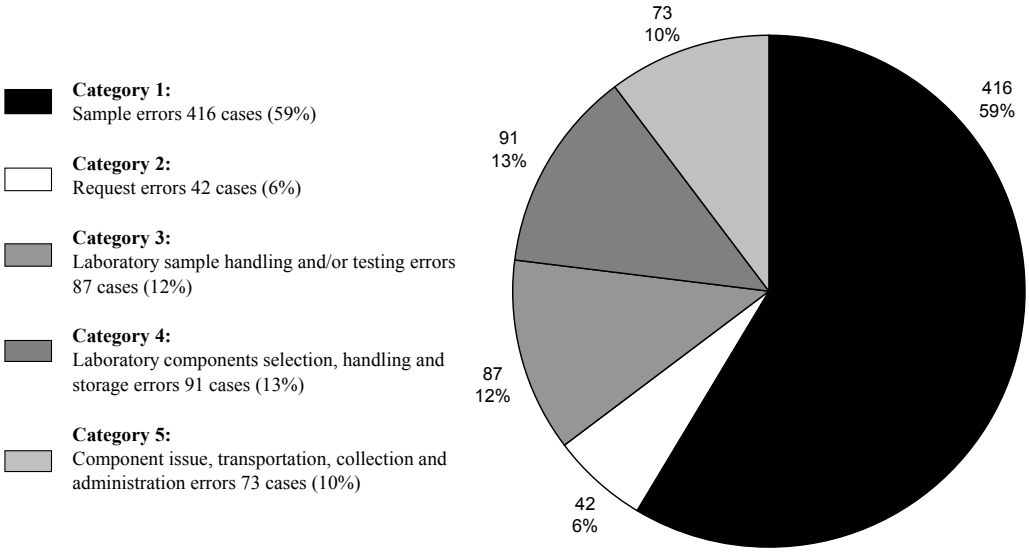
the preponderance of phlebotomy errors which are generally detected in the laboratory and reported internally. Laboratory "near misses" e.g. grouping errors are also well reported as these too are detected in the laboratory. Ward based and portering "near misses" are less likely to be captured by the current systems in most hospitals as these errors are corrected at the time of the event and the incident may not even be reported, or may not come to the attention of the person responsible for SHOT reporting in that hospital.

Categories of "near miss"

SHOT identifies five categories of "near miss" with a different form to be filled in depending on the category of each event. The chart below (figure 24) lists the five categories and the proportions of "near miss" events and actual numbers for the year 2001-2002.

Figure 24
Categories and proportions of "near miss" events

Total number of reports 709



Category 1: Sample errors - 416 cases

The proportion of sample errors has increased from 50% in 2000-2001 to 59% in the current reporting year. This may represent increased reporting of "near miss" events in the category in which it is easiest to gather data i.e. those which are picked up by BMSs working in the laboratory. This year 201 sample errors resulted from samples being labelled with the intended patient's details but which were subsequently found to contain blood from a different patient. Another 193 reports related to incidents in which the correct patient had been bled but the sample was labelled with another patient's details. In most of these cases (245) the error was identified by finding a different historical blood group in the blood bank records. In cases where the patient had not previously been grouped such errors would not be detected. In 48 instances the person who performed the phlebotomy realised later that they had made a mistake in identification of the patient and informed the laboratory. On 2 occasions the error was discovered at the final bedside check before administering the blood component.

All of these events occurred because of failure to follow local protocols and national guidelines for patient phlebotomy. If a patient positively confirms their name and date of birth, or if the hospital number and other

details are copied from the patient's wristband at the bedside immediately following the phlebotomy, such errors cannot not take place.

In 12 cases addressograph labels were used to label samples. This has been previously identified as a dangerous practice, as it is too easy to put the wrong label on a tube and there is a tendency to pre-label. National guidelines[6] state that addressograph labels should not be used for this purpose and a study of implementation of the guidelines has shown a favourable effect on patient safety[16].

Of these sample errors 248 were attributed to medical staff, 84 to nursing staff and 32 to phlebotomists. Another 2 samples were taken by medical students. This raises important questions as to what training and documentation of training should be in place for hospital personnel before they are permitted to take blood transfusion samples from patients.

125 samples were taken at times identified as outside routine working hours and 15% of sample errors were related to blood collected in A&E departments However lack of denominator data makes interpretation difficult.

It is interesting to note that at least 4 samples were wrongly labelled when a computer pick list for patient identification and generation of computerised request forms was used. Sample labelling was then copied from the computerised forms.

Category 2: Request errors - 42 cases

This category comprised 6% of the "near miss" reports. Nine cases were reported in which components were requested for the wrong patient and in 12 cases unsuitable components were requested for patients. In a further 9 cases the special requirements were not specified at the time of requesting. Nine of these errors involved telephoned requests. A recurring theme is that components are requested on the basis of erroneous laboratory results. There were 8 reports of inappropriate requests for red cells based on erroneous haemoglobin values, one of which might have resulted in disastrous over transfusion of a neonate. The erroneous results invariably arose from poor practice e.g. drip arm sampling, settling of blood in syringe, use of blood gas machine to determine haemoglobin level etc. Overall 34 of these request errors involved medical staff, 5 involved registered nursing staff and 3 other categories of staff.

Category 3: Laboratory sample handling/ testing errors - 87 cases

These comprised 12% of the total reported and involved qualified BMS staff in 72 cases, trainee BMSs in 8 cases, MLA in 2 cases, and a doctor in 1 case. Clerical and transcription errors accounted for 23 cases and 43 cases were caused by technical errors and failure to follow laboratory protocols.

There were 5 "near misses" relating to blood service errors. These were: supply of non irradiated blood (no Radsure™ label) when irradiated was requested: supply of K positive blood when K negative was requested twice (detected on cross match): missing of anti Jk^a antibody: incorrect anti-D quantification.

Category 4: Laboratory component selection, handling and storage errors - 91 cases

These accounted for 13% of all events reported, although most (27) were related to incorrect storage of components, mostly by non laboratory staff on the wards or during transportation, and subsequent wastage of the components involved.

A further 17 cases were instances where the laboratory issued components without ensuring that special requirements were fulfilled. By far the most commonly reported problem was a failure to issue irradiated components where these were necessary. These errors were identified at bedside checking. In this category 24 cases (26%) of problems occurred outside normal laboratory working hours.

Category 5: Component issue, transportation and patient identification errors - 73 cases

Collection of a component intended for the wrong patient has been identified in previous SHOT reports as the first error, which, if not detected at the final bedside check, results in a 'wrong blood to patient' episode. Local

protocols if based on national guidelines should state that when collecting a blood component from the issue area in blood bank, appropriate documentation should be brought bearing three unique identifiers for the intended recipient, i.e. the patient's name, date of birth and hospital number. If these three items of ID are properly checked it is impossible for the wrong component to be collected. Electronic systems for controlling release of blood from storage sites may also reduce these errors. This type of error accounted for 37 cases with the error being detected at the bedside in 30 cases.

The use of an electronic bar code reader on a ward prevented an error in one case reported this year. (Case 4)

Cases

Case 1
Two patients attending a gynaecology outpatients clinic had very similar surnames and the same first name. Patient 1 was admitted for bleeding problems and a group and screen sample was taken. The notes were requested from out-patients, but when a nurse went to collect them she picked up patient 2's notes by mistake. These notes were then used to label the samples which had been taken from the first patient. Fortunately patient 2 had a historical blood group on the blood bank computer which enabled the error to be detected.

This is a classic example of the danger of using hospital notes to label a blood sample and failing to follow the protocol which would involve asking the patient to state her name and date of birth, which would have then been put directly onto the sample tube. This kind of error is the most common reported "near miss".

Case 2
A patient's sample was sent to the laboratory with an incorrect date of birth and no hospital number. Because the date of birth was incorrect, the patient's computer record of irregular red cell allo-antibodies was not accessed. A doctor subsequently requested a cross-match on this sample for this patient. At this stage the error was detected. The doctor was asked to amend the sample and request accordingly. However the laboratory failed to re-register the patient and once again the antibody data was not accessed. The antibody screen was carried out manually and also on an automated instrument. Both gave a weak positive reaction that was regarded as negative. The cassette was discarded prior to the independent check, which was a breach of the SOP for manual antibody screening. The allo-antibodies were thus not detected and incompatible blood was selected. Shortly before the blood was issued, a further sample and cross-match request with all the correct details, including the correct date of birth and hospital number was fortuitously sent down from the ward and enabled the error to be detected.

This case shows how vital it is that all three unique identifiers are required before a sample can be accepted in the laboratory for grouping, screening and cross-match. Although the name was correct, the absence of a hospital number meant that the incorrect date of birth was not picked up. There was a subsequent breach of protocol in the antibody screening and these two errors compounded to produce a potential delayed haemolytic transfusion reaction.

Case 3

At a surgical pre-admission clinic patient 1, a young woman, was grouped as A RhD positive though her historical record showed her to be O RhD negative. On admission another sample was taken which, this time, grouped as O RhD negative and agreed with the historical record. Another female patient, patient 2, was admitted at the same time though we have no information about her blood group at that time. The post-operative sample labelled with patient 1's details was grouped as A RhD positive. The conclusion which was drawn from this was that patient 1 and patient 2 exchanged identities in order that patient 2 could have her surgery first.

Case 4
Blood was correctly grouped and screened but the wrong transfusion forms were put in with the wrong units so the form for ward A went with the unit for a patient on ward B. When ward A scanned the unit using an electronic hand held barcode reader it was detected that it was the wrong unit for the patient on the form. Both units were recalled and reissued correctly. An ABO incompatible transfusion was thus prevented by the use of an electronic barcode reader.

COMMENTARY

1. Special requirements are frequently missed especially when a patient's care is shared between different hospitals or hospital departments. Clear communication between doctors, nurses and blood bank staff is vital in these circumstances. In particular there is a frequent finding that irradiated blood components are not being provided for patients who require them. It would be advantageous if patients too were aware of special issues e.g. the presence of atypical antibodies or the need for irradiated or CMV negative blood components. In addition procedures should be in place to notify the laboratory of special requirements.

2. It is increasingly reported that erroneous laboratory results, in particular haemoglobin values, have contributed to incorrect and inappropriate requests for blood components.

3. Some hospitals do not require wristbands to be worn by children in intensive care units and special care baby units. This is an entirely unacceptable practice and is in breach of national guidelines. Neonates often share the same date of birth, may have no first name and may be siblings, hence some reliable means of identification such as a wrist/ankle bank or suitable adhesive label is essential.

4. Failure to follow protocols for patient identification at phlebotomy is a major problem This may reflect inadequate training of staff involved, particularly doctors who were involved in the vast majority of cases reported. It is possible that training has taken place but protocols are not being followed owing to a lack of understanding of the serious consequences of errors.

RECOMMENDATIONS

- **Patients should wherever possible be educated about their own special transfusion requirements e.g. irradiated components or special phenotype selection. The provision of patient held cards and suitable information will facilitate this.**

- **Hospital protocols must state that there must be no exceptions to the requirement for identity wristbands to be worn by all patients. This has implications for other aspects of clinical care and should be regularly audited.**

- **As recommended last year, all hospitals must have a training programme in place for phlebotomy which must include medical staff.**

12. ACUTE TRANSFUSION REACTIONS

Definition
Acute transfusion reactions are defined in this report as those occurring at any time up to 24 hours following a transfusion of blood or components, excluding cases of acute reactions due to incorrect component being transfused as these are covered in Chapter 10

This category accounted for 10.3% of non-infectious hazards reported and 10.1% of all hazards.
There were 6 outstanding reports from the previous reporting year for which 5 questionnaires were eventually received and are included in the analysis. 1 outstanding report was written off after the 6 month deadline had passed. For an explanation of the system of maintaining deadlines please see chapter 4 "Overall organisation and reporting system."
From 54 new initial reports there were 48 completed questionnaires. The 6 outstanding questionnaires will be included in next year's analysis. Additionally 5 reports did not fit the definition of ATR and have been withdrawn, 4 by the analyst and 1 by the reporter.
This chapter highlights the main findings from 48 completed questionnaires.

There were 7 deaths in this group; 1 probably related to the transfusion, 1 possibly related to the transfusion and 5 unrelated to the transfusion.

Gender (48 reports)

Males	27
Females	21(one female recipient was involved in 2 reports)

Age (48 reports)

Age range	2 days to 93 years
Median	67 years

Components implicated (48 reports)

Red cells	17	
Platelets and cryoprecipitate	1	
Platelets	10	(4 from apheresis and 6 from pooled buffy coats)
Platelets and fresh frozen plasma	1	(pooled buffy coat platelets)
Fresh frozen plasma	18	(1 solvent detergent treated)
Cryodepleted fresh frozen plasma	1	

Reactions in which red cells were implicated

There were 17 cases, with one death probably related to the transfusion, one possibly related to the transfusion and 2 deaths due to the underlying disease. 13 reactions occurred during the transfusion, 3 within 2 hours of completing the transfusion and 1 within 7 hours of completing the transfusion. The following reactions were seen:

Table 28
Reactions in which red cells were implicated

Reaction type	Number of cases
Haemolytic or incompatibility reaction	8
Anaphylactic[+]	2
Allergic[++]	5
Neutropenia	1
Hypoxia and acidosis (neonate)	1

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

Haemolytic or Incompatibility Reactions

In 6 cases, red cell alloantibodies or autoantibodies were thought to have contributed to the reaction.

Case 1
A 74 year old female with high grade B-NHL and a previous transfusion history, was found on pre-transfusion testing to have a positive DAT (C3d) and a weak antibody in her serum showing no specificity. A presumptive diagnosis of autoimmune haemolysis was made. These findings were confirmed by the reference laboratory who provided 2 units of red cells that were weakly incompatible by IAT crossmatch. The patient became febrile with a tachycardia and hypertension during the transfusion, which was stopped after 60mL. Post-transfusion, her haemoglobin fell and she had circulating spherocytes. The post-transfusion serum reacted more strongly with panel cells than with the patient's own cells and was referred to the International Blood Group Reference Laboratory (IBGRL), who found anti-Vel. The patient received further units, unselected for Vel, prior to the receipt of the IBGRL findings and suffered no further reactions. However she was receiving steroids for a presumptive diagnosis of autoimmune haemolysis in association with her B-NHL. It is not known whether the anti-Vel was an autoantibody or alloantibody, although IBGRL favoured the latter explanation. The patient died 3 weeks later from her underlying disease.

Case 2
A 69 year old female with acute myelofibrosis/acute myeloid leukaemia was transfused 2 units of red cells for her anaemia. She had received 8 units of red cells within the preceding 4 weeks and the pre-transfusion sample, taken within 48 hours of the reported transfusion, showed a positive DAT (IgG) but a negative serum antibody screen. 3-4 hours after the completion of the transfusion, she collapsed at home with chest pain and dyspnoea. She was taken to another hospital, where she was admitted to ICU with haemoglobinuria, other biochemical evidence of haemolysis and deteriorating renal function and subsequently died.
Retrospectively, her pre-transfusion serum contained an anti-C, detectable only using papain-treated red cells in the IAT and the eluate contained an anti-C-like antibody and an anti-e-like antibody. She had been transfused with R_1r and R_2r units and post-transfusion there was no detectable antibody in her serum and the eluate again contained an anti-C-like antibody and an anti-e-like antibody. Her Rh genotype was suggested to be R_1R_2 on the basis of polymerase chain reaction. Bacterial cultures of the 2 units and the patient were negative.
The patient was found to have mitral stenosis at post-mortem but was thought to have died as a result of haemolysis. The most likely explanation is an exacerbation of autoimmune haemolysis as a result of the transfusion. Autoimmune haemolysis could also have contributed to her excessive red cell transfusion requirements over the 4 weeks prior to her demise.

Case 3
A 10 year old girl had undergone an unrelated (cord) stem cell transplant for acute myeloid leukaemia 2 months earlier at another centre and post-transplant had been diagnosed to have an autoimmune haemolytic anaemia. The reporting hospital had not been provided with any details of her previous transfusion record including the donor's and recipient's original ABO groups. On this occasion she was grouped as O, with a positive DAT (IgG and C) and positive antibody screen. All further testing was performed by the reference laboratory but no details are available. During the reported transfusion, she developed back pain and dark urine and was confirmed to have haemoglobinuria and hyperbilirubinaemia. She was immediately transferred back to the transplant centre.
It was assumed that the patient had suffered an exacerbation of the underlying autoimmune haemolysis but further information has not been available.

Case 4
A 76 year old female with probable myelodysplasia and a weakly positive DAT (IgG) was found to have an antibody in her serum, reacting with all panel cells but not her own cells. These reactions were not observed using plasma and units were issued on the basis of their compatibility using plasma for crossmatching. The patient became febrile and hypotensive during the transfusion which was stopped after 100mL. Investigations confirmed haemolysis but no deterioration of renal function. Subsequent testing at the reference laboratory confirmed the presence of an anti-Vel, reactive only in serum.
The laboratory now recommend that all transfusion reactions are investigated using both serum and plasma.

Case 5
A 66 year old female with acute myeloid leukaemia and sepsis, transfused uneventfully 12 days earlier, had a positive DAT (IgG and C3d) and antibody screen on pre-transfusion testing. The sample was referred and an anti-E was identified in the serum following alloabsorption with Rh identical and Jk^a negative cells. The patient was transfused, 2 days after the sample was taken, with E negative units and became febrile and hypotensive during the first unit, which was stopped. The post-transfusion sample contained anti-E+Jk^a and the unit transfused was Jk^a positive. The anti-Jk^a was not detected on retrospective retesting of the pre-transfusion sample.

Case 6
A 93 year old male, known to have anti-k and to have recently undergone an abdominal aortic aneurysm repair, was readmitted as an emergency with bleeding from an infected surgical site. He was transfused as an emergency in casualty with 1 unit of "emergency O neg" (group O, rr, K negative) red cells during the time the laboratory was being provided with a sample and accessing the historical records. The clinicians in casualty were made aware of the need for k negative blood but the patient required resuscitation with 3 further units of k incompatible blood before compatible units could be provided. The patient complained of loin pain during the initial transfusion and died 48 hours after admission. It is not clear to what extent the haemolysis contributed to his death.

In the following 2 cases, although anti-Jk^a was demonstrated following the transfusions, it is not clear whether the antibody had contributed to the reaction.

Case 7
A 43 year old male with a mixed connective tissue disorder, had bled following a renal biopsy and had received 11 units of red cells in the 6 days prior to the reported transfusion. There was no other known transfusion history although the patient had been found to have a positive DAT in 1995. The pre-transfusion sample taken less than 48 hours before the reported transfusion showed a negative DAT and antibody screen. The patient developed fever and rigors during the transfusion and the post-transfusion sample showed a positive DAT (IgG) and the serum contained anti-Jk^a. There was a modest rise in bilirubin from 8 to 18umol/L but the haemoglobin remained stable. No bacterial culture was performed on the 4 units of red cells given, but coagulase negative staphylococci were cultured from the tip of the arterial line and some of the blood cultures. The patient had developed 2 other febrile episodes in the 48 hours preceding the reported transfusion and the "transfusion reaction" may have been due to the infected arterial catheter, rather than the anti-Jk^a.
No eluate was performed on the post-transfusion sample and the units given were not typed for Jk^a, to confirm that a Jk^a incompatible unit had been transfused. Although no previous transfusion history had been elicited, it is extremely unlikely that the detected anti-Jk^a represented a primary response to transfusions given within a 6 day period.

Case 8
A 68 year old male with myelofibrosis and no previous transfusion history developed dark urine during a 3 unit red cell transfusion and was confirmed to have haemoglobinuria. His haemoglobin initially rose from 80g/L to 112g/L but had fallen to 88g/L 48 hours later. His bilirubin rose from 41µmol/L to 138µmol/L over the same period. His pre- and post-transfusion samples had negative antibody screens and negative DATs, but a sample taken 18 days after the reaction contained an anti-Jk^a, reactive only with homozygous cells. 2 of the 3 units transfused were Jk^a positive. The patient was transfused 4 months later when his antibody screen was negative. He received 2 units matched for K, Jk^a, Fy^a and S but again developed haemoglobinuria with no apparent serological cause.
No explanation was found for the haemolysis, except for a degree of hypersplenism.

Transfusion Related Alloimmune Neutropenia

Case 9
A 2.2kg male infant born at term was diagnosed as having transposition of the great vessels. He underwent a switch procedure at 4 weeks and the operation proceeded without complication. On the 2nd post operative day, 80mL of plasma reduced blood containing approximately 12.5mL/kg of plasma was transfused over 4 hours. Preoperative and postoperative white cell counts (WCC) were normal. 2 hours before the transfusion the WCC was 7.4 x 10^9/L with a normal differential. 2 hours post-transfusion the WCC had fallen to 0.7 x 10^9/L

(neutrophils 0.06, monocytes 0.08, lymphocytes 0.48 and eosinophils 0.01 x 10^9/L). The count was repeated twice with the same results. The neutropenia persisted and 48 hours post-transfusion a bone marrow was performed. This showed active myelopoiesis to the stage of metamyelocytes but no band or segmented forms. Treatment was started with daily Granulocyte Colony Stimulating Factor (G-CSF) 3 ug/kg sc and the neutrophil count returned to normal at 5 days post-transfusion. The chest X-ray showed no infiltrates and there was no evidence of respiratory distress syndrome to suggest Transfusion Related Acute Lung Injury.
Plasma from the donor unit was tested for HLA and neutrophil antibodies. A strongly reacting antibody to human neutrophil antigen 1b (HNA-1b) was detected with chemiluminescence, immunofluorescence and monoclonal antibody capture assays. The patient had a genotype of HNA-1a1b.
The donor was an untransfused multiparous female aged 48 years. Her last pregnancy was 19 years before the current donation and there was no history suggestive of alloimmune thrombocytopenia. Her genotype was HNA-1a1a and her husband's genotype was HNA-1b1b.

This case has been fully documented in the Lancet[17] and is reported here with the permission of Dr JP Wallis.

Anaphylactic/anaphylactoid reactions

Two patients developed anaphylactic/anaphylactoid reactions during red cell transfusions, and both survived with no ill effects. One was tested for IgA deficiency, with negative results and has subsequently been uneventfully transfused with washed red cells.

Allergic

There were 4 apparent allergic reactions in this group.

Hypoxia and Acidosis in a Neonate

There was one case reported of a 5 month old girl with pneumonia, who became increasingly tachypnoeic and acidotic after receiving 15mL/kg red cells with a pH of 6.9. This pH is within the expected range for red cells and would not have contributed to the acidosis.

Reactions in which FFP was implicated

There were 19 reports in this group, (including the report implicating cryodepleted FFP) of which 16 occurred during the transfusion, 2 within 2 hours and 1 between 2 and 7 hours of completing the transfusion. The following reactions were seen:

Table 29
Reactions in which FFP was implicated

Reaction Type	Number
Anaphylactic	7
Allergic	9
Febrile	1
Hypotension	1
Cardiac failure	1

Anaphylactic/anaphylactoid

There were 7 patients in this category, all of whom recovered from the reaction, but one of whom later died unrelated to the transfusion. All but one patient received a combination of hydrocortisone and adrenaline. One patient developed oliguria and required additional inotropic support and a second with bronchospasm required additional bronchodilators and oxygen.
Two patients were investigated for IgA deficiency, with negative findings; in 1, the nature of the reaction was confirmed with an elevated plasma tryptase level and the second patient had Gm1 antibodies. Four patients had respiratory symptoms, of whom 2 had a chest X-ray performed, the results of which are unfortunately not available. Another patient, although reported to be asymptomatic was found to have a reduced O_2 saturation.
In 1 patient, there was no clear indication for prescribing FFP.

Case 10
A 52 year old female was undergoing plasmapheresis with cryodepleted FFP for thrombotic thrombocytopenic purpura when, towards the end of the procedure, she developed a rash and became hypoxic and hypotensive. She was resuscitated with adrenaline and hydrocortisone and has since been receiving SD-FFP (pooled) as replacement plasma. The patient had a normal IgA level but anti-Gm1 antibodies were found in her plasma.

Case 11
A 2 day old term female who had had a traumatic delivery, received blood components for a coagulopathy and subaponeurotic haemorrhage. The patient had no untoward effects from the first 3 aliquots of a dedicated FFP paedipack, and had also received red cells, platelets and cryoprecipitate. At the end of receiving the last aliquot of 32mL plasma, she developed a rash, dyspnoea, bradycardia and hypotension. A chest X-ray showed no infiltrates and she recovered following hydrocortisone. Further transfusions were given uneventfully with hydrocortisone cover.

Allergic reactions (mild)

There were 9 patients in this group, 3 with a rash and 6 with dyspnoea and a fever. Two of the latter had chest X-rays performed; 1 not reported and the second with negative findings.

Hypotension

Case 12
A 73 year old male with chronic renal failure received 1 unit of FFP whilst having his vascular line changed (no coagulation results given). He became hypotensive after receiving 100mL FFP and was treated with antihistamines and a diuretic. It is not known whether he was being treated with angiotensin converting enzyme (ACE) inhibitors.

Cardiac failure/ myocardial infarct

Case 13
A 73 year old male, with metastatic rectal carcinoma and on warfarin, was given 3 units of FFP prior to an emergency Hickman line removal. Two hours later he became dyspnoeic, was diagnosed to have left ventricular failure and later found to have a raised troponin level, consistent with a myocardial infarct.

Inappropriate use of FFP

In 12 of the 19 reports, sufficient information was provided to suggest that the use of FFP was justified.

The use of FFP could not be justified in 2 patients; 1 was overdosed with warfarin, but was not bleeding nor was there an imminent procedure and the second received FFP post-operatively, when there was no active bleeding and no prothrombin time (PT) had been performed. Five patients, with no medical reason for a bleeding tendency, received FFP during elective procedures when less than 6 units of red cells were transfused. No coagulation findings were reported.

Reactions in which a combination of components was implicated

There was 1 case of fluid overload and 1 allergic reaction.

Case 14
A 39 year old female with acute myeloid leukaemia (M3) had received 4 units red cells, 19 units cryoprecipitate, 8 units of FFP and 1 pool of buffy coat derived platelets. Six hours later she developed dyspnoea, hypoxia (O_2 sats. 92%) and tachypnoea and the chest X-ray was consistent with pulmonary oedema. She made a full recovery with oxygen, diuretics, bronchodilators and hydrocortisone but developed a similar episode following another transfusion of multiple units of plasma containing components.
The reporter was uncertain as to whether this reaction represented fluid overload or TRALI. However since investigations for TRALI were negative and the patient had received several litres blood components on each occasion and made a rapid recovery, this case has been classified as fluid overload by the SHOT team.

Case 15
A 77 year old female received 1 pool of buffy coat platelets and 4 units of FFP at the time of coronary artery bypass grafting. No details of coagulation studies are provided. Two hours later she developed a rash, angioedema, dyspnoea and hypoxia. She was treated with hydrocortisone and nebulised bronchodilators. Investigations revealed reduced complement levels and a raised plasma tryptase level in keeping with an allergic reaction.

Reactions in which platelets were implicated

There were 10 reactions in this group, of which 7 occurred during the transfusion, 2 within 2 hours and 1 between 2 and 7 hours following the transfusion. One of these patients patient died from haemorrhage, despite platelet transfusion support and was subsequently found to be alloimmunised to anti-HPA5b and a second patient died unrelated to the transfusion. All other patients recovered from their reactions without sequelae.

Table 30
Reactions in which platelets were implicated

Reaction Type	Number of cases
Anaphylactic	3
Allergic	7

Nine of the 10 patients had received previous transfusion support.

No further immunological investigations were performed on the 3 patients with anaphylactic/anaphylactoid reactions, despite the fact that 2 of the 3 had not previously received plasma or platelets and could have been IgA deficient. 1 patient became hypoxic with an O_2 saturation of 92%

Five patients with allergic reactions had further immunological investigations.
Two patients with allergic reactions were found to have anti-HPA antibodies and had no further reactions on receipt of HPA matched platelet donations. It is not known whether these patients were refractory to random platelet concentrates or to what extent the transfusion of HPA matched platelets improved the post transfusion increments. One patient with rash and dyspnoea was found to have Gm antibodies but the subsequent tolerance of platelet transfusion is unknown. In 1 case the donor plasma was found to contain multispecific HLA Class II antibodies. Finally, 1 recipient was found to have anti-Chido.

One patient with repeated allergic reactions consisting of rash, dyspnoea and tachycardia was documented to have no further problems when receiving platelets in suspension medium rather than plasma.

Six of the 10 reactions were accompanied by dyspnoea, including the case in which the donor plasma contained HLA Class II antibodies. All required treatment with hydrocortisone and 2 also received nebulised bronchodilators and oxygen. One chest X-ray was performed in this group with negative findings.

Response times

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

Table 31
Time taken for patient to be reviewed by a doctor from being called

Response Times	Red cells (17)	FFP (21)*	Platelets (10)
Stat	5	12	5
< 30 minutes	5	5	4
< 60 minutes	2		
> 60 minutes	1		
Data not available	2	3	
Late reaction	1		1
Not seen	1	1	
Total	17	21	10
Involvement of Haematologist	**14**	**7**	**9**

* includes cases in which other components were transfused

Patient Monitoring

In 18/48 cases, the reporter could not access records of nursing observations taken during the transfusions. Records of observations made during platelet transfusions outside an intensive care setting were notably absent. The frequency of patient observations met the standards given in the BCSH guideline[6] in only 6/11 red cell and 7/15 FFP transfusions.

Table 32
Frequency of patient monitoring during transfusion

Frequency monitoring	Red Cells (17)	FFP (21)*	Platelets (10)
Constant (ICU)	**1**	**2**	**2**
Pre / 15 min post	**5**	**5**	**0**
30 minute intervals	**4**	**5**	**0**
Hourly	**1**	**0**	**0**
> hourly/none	**0**	**3**	**2**
Not available	**6**	**6**	**6**
Total	**17**	**21**	**10**

* includes cases in which other components were transfused

Investigations

3/12 anaphylactic reactions were investigated. 1/2 investigations involving red cells were negative as were the 2/7 investigated reactions involving FFP. No investigations were performed on recipients of platelets who suffered this type of reaction.

Of the allergic reactions, 1/3 involving red cells was investigated with a negative outcome. Investigations of 5/10 allergic reactions to FFP (in 2 cases given in conjunction with other components) revealed positive findings in 2/5 transfusions. In 1 case HLA antibodies were found in the patient and at least 1 of the donors and 1 patient had Gm antibodies. 5/7 patients with allergic reactions to platelets were investigated with positive findings as indicated above.

Changes made to procedures

The laboratory reporting case 4, an acute haemolytic reaction attributed to an anti-Vel reactive only in serum, has changed its protocol for investigating transfusion reactions to include the requirement for both serum and plasma samples.
Three other laboratories took action as a result of reporting acute transfusion reactions to FFP. Two hospitals where the reaction occurred when FFP was inappropriately prescribed have reaudited the usage of this component as part of an educational programme. A third hospital in which a patient suffered an anaphylactic reaction to FFP now requires that a haematologist is contacted to advise upon the management of reactions to all blood components.

Reporting of acute transfusion reactions

All but 1 acute transfusion reactions were reported to the hospital laboratory. 82% of reactions involving red cells were reported to the Hospital Transfusion Committee and 76% and 70% of those involving FFP and platelets. Reactions were reported to the local Transfusion Centre when samples were sent for further investigation.

Table 33
Reporting of reactions to the Hospital Transfusion Committee, Hospital Laboratory and the local Transfusion Centre

Reported to	Red cells (17)	FFP* (21)	Platelets (10)
Hospital Transfusion Committee	14	16	7
Hospital laboratory	16	20	10
Transfusion centre	12	10	8

* includes cases in which both FFP and platelets were transfused

COMMENTARY

- The majority of acute transfusion reactions (31/48) were due to FFP and platelets, as in previous years, with 79% (27/34) allergic or anaphylactic reactions due to these 2 components.
- It is apparent that FFP has the highest risk of causing an acute reaction and yet is often inappropriately prescribed[10].
- Haematologists were frequently not involved in the management or investigations of acute reactions involving FFP.
- A minority of transfusions, particularly those involving platelets, were monitored in accordance with BCSH recommendations[6].
- In 4/12 cases where a haemolytic transfusion reaction was either suspected or confirmed, the DAT was positive with the cells being coated with IgG, and no eluate or additional investigations were performed.
- There were 5 cases of anaphylactic/anaphylactoid reactions in patients who had not been previously exposed to plasma containing components and who were not investigated for IgA deficiency.
- Investigations of allergic transfusion reactions were performed in the majority of recipients of plasma containing components. In 3/5 platelet recipients, investigations revealing HPA and/or HLA antibodies influenced the future transfusion support of the patient.
- Alloimmune neutropenia, in the absence of clinical features of transfusion-related acute transfusion injury, has been reported as an additional complication of transfusing plasma containing antibodies against human neutrophil antigens

RECOMMENDATIONS

- **Patients receiving any blood component must be monitored to detect an acute reaction. Patients must be checked prior to the transfusion of each component and 15 minutes after its commencement.**

- **Patients who have had a severe allergic reaction (anaphylactic/anaphylactoid) should be investigated for IgA deficiency.**

- **Where plasma samples are routinely used for pre-transfusion testing, it is recommended that serum samples are also used in the investigation of suspected transfusion reactions.**

- **Particular care should be taken when providing blood for patients with a positive DAT, who are known to have an autoimmune haemolytic anaemia or have been recently transfused. Referral to a reference centre, if time allows, should be considered.**

- **There is a need for a guideline dealing with the investigation of all acute transfusion reactions.**

- **There is continued evidence of inappropriate use of clinical FFP[10], and further local audits and educational programmes should be encouraged. A revised BCSH guideline is expected during 2003; in the meantime, existing BCSH guidelines[8, 9] should be followed.**

- **The options for using untransfused males as donors of clinical FFP and for suspending platelets in plasma-free media should be pursued by the UK blood services.**

- **When the care of patients with haematological disorders requiring transfusion support is shared, there is a risk that not all pertinent transfusion history will be available to both sites. In the absence of networked pathology information systems, it is essential that local procedures are devised for adequate communication between laboratory as well as clinical teams.**

13. DELAYED TRANSFUSION REACTIONS

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

This category accounted for 9.6% of non-infectious hazards reported and 9.5% of all hazards.
Forty-six new initial reports were received and 3 were brought forward from the previous year. Five additional reports were received which were not included in the analysis for this chapter. Two of these were withdrawn by the reporters following further investigation, 1 was withdrawn by SHOT staff on review, 1 was an incorrect component transfused and is included in that chapter and 1 was "written off" when it became clear that a completed questionnaire would not be returned by the reporter. Two reports received during the reporting period are still awaiting completion of a questionnaire and will be presented next year.
This chapter highlights the main findings from 47 completed questionnaires (44 from the current reporting year).

Age and sex

Age (46 reports)

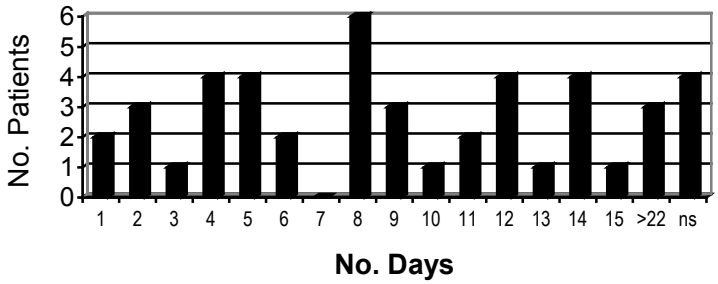
Age range	17 – 91 years
Median age	67 years

Sex (47 reports)

Males	20
Females	27

Figure 25 shows the interval in days between the implicated transfusion and signs or symptoms of a DHTR.

Figure 25
Interval between transfusion and symptoms



Range: 1 to 40
Median: 8

Reactions reported

There were 9 deaths in this group, of which 2 were thought to be definitely due to and 1 probably due to the transfusion reaction. One further patient suffered some renal impairment and another required admission to ICU and renal dialysis. The remaining patients suffered minor or no morbidity.

All reactions were probably caused by the administration of allogeneic red cells, although not all reports fit the classical definition of a delayed haemolytic transfusion reaction. Those where the antibody was detectable retrospectively in the pre-transfusion sample and possibly those where signs of haemolysis were noted within 2 or 3 days of the transfusion may well have had mild, ongoing extravascular haemolysis during or soon after the

transfusion. In 2 cases no antibody was detected pre or post transfusion. One of these (case 45, male) had a clear-cut haemolytic reaction and a positive direct antiglobulin test when tested 4 days after transfusion, but had no known history of previous transfusion. The second was a patient with sickle cell disease (case 27) who had a well-demonstrated haemolytic episode with a negative DAT, and required ICU admission and renal dialysis; this was probably due to hyper-haemolysis associated with SCD, rather than a DHTR, although insufficient detail was provided about the investigations undertaken to be conclusive. In a further 2 emergency cases (46 and 47), no pre-transfusion testing was performed, but antibodies were detected retrospectively in the pre-transfusion sample; again, there was insufficient information provided to determine when signs of haemolysis developed (a fall in Hb and an isolated rise in bilirubin, respectively).

Seventy new antibodies were identified in 42 patients. In one (case 28), the antibody was detected only in the eluate and in a second (case 1) no specificity was assigned.

Four cases had no reported history of previous transfusion or pregnancy. In one of these (case 10) the reaction was probably due to primary sensitisation, the antibody being detected 40 days post transfusion. In the other three cases (all male patients) the antibodies were found within 10 days of the transfusion and it must, therefore, be assumed that these patients had received previous transfusions unknown to the reporter.

Six patients had a positive antibody screen before transfusion. In three emergency situations crossmatch compatible blood was transfused before full investigation of a positive antibody screen was complete. Anti-Jk^a reacting only with Jk(a+b-) cells, at least by the column IAT technique in use (one DiaMed, one BioVue), was missed in the crossmatch in two of these patients (cases 18 and 35). In case 35, a newly developed anti-Fy^b was also identified post transfusion; it is unclear to what extent the missed pre-existing anti-Jk^a and the newly developed anti-Fy^b contributed to the reaction, although no signs of haemolysis were noted until 9 days post-transfusion. In the third of the emergencies (case 38, described in detail later), anti-c+E+Jk^a was retrospectively identified in a pre-transfusion sample by a reference laboratory, but other than a positive DAT, no symptoms of haemolysis were noted. In 2 other cases, appropriately phenotyped blood was transfused but further antibodies developed (cases 25, 36). In one report (case 31), phenotyped blood was selected for the antibody identified, but a 2^{nd} weak antibody was retrospectively identified in the pre-transfusion sample. In addition to case 27, already described, 6 further patients had a negative DAT post-transfusion. All had clear-cut haemolytic reactions (grade 3 or 4) with identifiable red cell antibodies.

Urgency of transfusion requirement

The transfusion was said to be routine in 28 patients and an emergency in 19.

New post transfusion antibodies

Table 34 shows the specificity of all new antibodies detected post-transfusion and table 35 antibodies in individual patients. The data include antibodies missed that should have been detected pre-transfusion, but not those that were undetected because pre-transfusion testing was omitted due to the emergency nature of the request.

Table 34
Specificity of new antibodies detected post-transfusion

Antibody specificity by blood group system	Number of cases	Sole new antibody
Kidd		
Jk^a	17	10
Jk^b	9	6 (1 detected in eluate only)
Rh		
c	11	1*
E	10	1*
D	2	2
C	2	
C^w	2	
e	1	
Duffy		
Fy^a	6	2
Fy^b	1	
$?Fy^3$	1	
Kell		
K	2	1
MNSs		
S	1	
s	1	
Other		
A_1	1	
Bg	1	
P_1	1	
Lu^a	1	

*In addition, there were 4 examples of anti-c+E reported.

Table 35
New post-transfusion antibodies in individual patients
(Cases in bold type indicate those that resulted in mortality)

Case No	Antibody (ies)	Comment
1	UI	
2	Jk^b	
3	D	
4	Jk^a+C^w	Detected by enzyme or enzyme IAT only
5	Jk^b	
6	Jk^a	
7	**c+E**	
8	Jk^a	
9	E	Anti-E detected in eluate
10	Jk^a	
11	Fy^a	
12	c+E	
13	**c+UI+cold reacting Antibody**	Anti-c in eluate
14	Jk^a	
15	c	
16	c+E+K	
17	Jk^a	
18	Jk^a	Pre-transfusion screen positive, ID panel not performed
19	Fy^a+E+Bg	Anti-E + anti-Fy^a detected in eluate
20	**c+E+Jk^b**	
21	K	
22	C+E+s+Jk^b+?Fy^3	
23	Jk^b	
24	c+E	Anti-E detected in eluate
25	c+S	Pre-transfusion anti-Fy^a
26	c+E	Record of anti-c at reference centre, but unknown to hospital
27	none	Negative DAT post-transfusion. SCD patient with probable hyperhaemolysis
28	Jk^b	Detected in eluate only
29	Jk^a+e	
30	Jk^b	
31	Jk^a	Pre-transfusion anti-E. Anti-Jk^a missed pre-transfusion, detectable vs Jk(a+b-) cells only.
32	A_1	? Passively acquired from FFP or platelets.
33	$Jk^b+Fy^a+C^w$	
34	Jk^b	Enzyme only antibody – identified by reference laboratory
35	Fy^b+Jk^a	Pre-transfusion anti-c + other unidentified antibody
36	$C+Jk^a+Fy^a$+UI	Pre-transfusion anti-E
37	Jk^a	
38	$c+E+Jk^a$	Pre-transfusion screen positive with non-specific reactions by CRRS*; negative by DiaMed
39	Jk^a	
40	Fy^a	
41	$c+Jk^a+Lu^a$	
42	D	
43	Jk^a+Fy^a	
44	Jk^a	Missed pre-transfusion by automated technique – detected retrospectively by manual technique
45	none	No known transfusion history
46	none	Pre-existing anti-c+E. No pre-transfusion testing performed.
47	none	Pre-existing anti-K. No pre-transfusion testing performed.

***** Capture R Ready Screen

Severity of reaction/ clinical sequelae

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

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

Group 1
There were 8 patients in this group. Two had falling Hb levels but this was probably related to their underlying condition. All survived with no sequelae.

Group 2
There were 11 patients in this group, of whom 4 survived with no long-term complications. Three required further transfusion due to their falling Hb (attributable to the DHTR), and the other four died from unrelated causes.

Group 3
There were 24 patients in this group, of whom 11 survived with no sequelae. One death (case 13) was definitely related to the transfusion and is described below. Two required admission to the High Dependency Unit, but suffered no long-term ill effects. One had his planned operation postponed. Six required further transfusion as a result of a falling Hb (attributable to the DHTR), but otherwise survived with no ill effects. The remaining two died of unrelated causes. One further case (47) remained on ICU at the time of reporting due to his underlying condition.

Group 4
There were four patients in this group. Two of them died, one definitely and one probably as a result of the DHTR and these cases are described below. The third required ICU admission and dialysis and the fourth patient had his discharge delayed by eight days, but both survived with no long-term ill effects.

Table 36
Individual new antibodies grouped by severity
(Cases in bold type are those that resulted in mortality)

Group 1		Group 2		Group 3				Group 4	
Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity	Case No.	Ab specificity
10	Jk^a	2	Jk^b	1	UI	21	K	7	**c+E**
12	c+E	9	E	3	D	22	$C+E+s+Jk^b+?Fy^3$	20	**c+E+Jk^b**
28	Jk^b	11	Fy^a	4	Jk^a+C^w	23	Jk^b	25	c+E
29	Jk^a+e	14	Jk^a	5	Jk^b	24	c+E	27	none
38	$c+E+Jk^a$	30	Jk^b	6	Jk^a	26	c+E		
39	Jk^a	31	Jk^a	8	Jk^a	33	$Jk^b+Fy^a+C^w$		
41	$c+Jk^a+Lu^a$	32	A_1	13	**c+UI**	34	Jk^b		
44	Jk^a	40	Fy^a	15	c	35	Fy^b+Jk^a		
		42	D	16	c+E+K	36	$C+Jk^a+Fy^a$+UI		
		43	Jk^a+Fy^a	17	Jk^a	37	Jk^a		
				18	Jk^a	45	none		
				19	Fy^a+E+Bg				

Case reports of deaths attributable to the DHTR

Case 7
A 65 year old male patient had an anterior resection for carcinoma of the colon and was later taken back to theatre for removal of an intra-abdominal haematoma. He had been transfused with several units of red cells, FFP and platelets over a 3 day period. Eight days following his first transfusion the patient had a fever, jaundice and red urine and his Hb fell to 40g/L. He underwent a third laparotomy for presumed internal bleeding and was transfused 5 units of red cells.

Pre-transfusion antibody screening performed by routine BioVue IAT on plasma samples taken on days 3 and 6 following the initial transfusion were negative. The day 6 sample is believed to have been used for an immediate-spin crossmatch for his third laparotomy. Post-operatively, the patient was admitted to ICU and required renal dialysis, but died three days later with metabolic acidosis, acute renal failure, episodes of bradycardia and hypotension. Meanwhile post transfusion serology on day 9 revealed anti-c+E by BioVue IAT and 2-stage enzyme and a positive DAT with anti-IgG. Retrospective testing of the pre-transfusion samples still showed negative antibody screens, although it was not stated in the report by which techniques this result was obtained or whether it was confirmed by the reference laboratory.

As a result of this episode, there has been a recommended change in practice, relating to increased awareness of DHTR causing red urine, jaundice and falling Hb. The case was also reported to the National Confidential Enquiry into Perioperative Deaths (CEPOD). Current BCSH guidelines[13] recommend testing a sample taken within 24 hours of the intended transfusion if the patient has been transfused within the previous 3-14 days. A sample taken on day 7 or 8 may have revealed the antibodies before the transfusion of the subsequent 5 units on day 8. Such a sample would presumably have been sent if the symptoms of DHTR had been recognised.

Case 20

A 77 year old female patient with ischaemic heart disease and atrial fibrillation was admitted with gastrointestinal bleeding secondary to excessive warfarinisation. She was transfused with 4 units of red cells as an emergency. Pre-transfusion antibody screening by routine BioVue IAT was negative (DAT not performed) and was followed by a routine BioVue IAT crossmatch. Eight days post-transfusion the patient developed a fever, chills, jaundice and a falling Hb. Post-transfusion testing by BioVue IAT and enzyme and by the blood service reference laboratory, revealed anti-c+E+Jk^a and a positive DAT with anti-C3 only. Retrospective testing of the pre-transfusion sample by both the hospital laboratory and the reference laboratory gave negative results. The patient was monitored on the ward awaiting a supply of compatible red cells from the NBS, but de-compensated, suffered a cardiac arrest and died before blood was available. Although the patient had pre-existing cardiac disease, the reporter felt that the anaemia caused by the DHTR probably contributed to the death.

The blood service had a previous record of anti-E for this patient and the reporter feels that having this information would have meant that antigen-negative blood would have been selected. The patient was presumably R_1R_1 and therefore R_1R_1 may have been selected had the history of anti-E been known. Blood selected for Rh-compatibility would not, of course, have prevented the development of anti-Jk^a. Although the positive DAT was caused by C3 only (suggesting coating with anti-Jk^a rather than anti-c or anti-E), one cannot be certain which specificity or combination of specificities contributed to the DHTR. Another point to be highlighted by this case was the lack of appreciation of the severity of the anaemia which, had it been realised, pre-transfusion testing could have been accelerated.

Case 13

A 51 year old female patient with vaginal bleeding had been transfused with four units of red cells on Day 1 and three units on Day 4. Pre-transfusion antibody screening on Day 4 by BioVue IAT (rapid/urgent technique) using a plasma sample was negative (DAT not performed) and was followed by a routine BioVue crossmatch. On Day 6 a new sample was received for pre-op hysterectomy and it was noted that the patient had received two recent transfusions.

There was a delay in processing the Day 6 specimen, due to the details being typed into the computer with the wrong hospital number. On testing the following day, the antibody screen was positive; manual BioVue testing using several panels of cells revealed possible anti-c and what appeared to be a cold auto-antibody. A subsequent sample suggested anti-c and anti-P_1 and although the DAT was positive, so was the negative control, and the patient's red cells typed positive for the c and P_1 antigens. The phenotypes were repeated at 37^{o}C (as it was thought that the cold agglutinins were interfering with the results) and were still positive. Further samples were requested and kept at 37^{o}C for testing the following morning. On Day 8, following repeat testing at 37^{o}C, a further sample was requested for referral to the blood service reference laboratory.

On Day 8 the ward and the blood bank were informed by the haematology laboratory that the patient's Hb was 40g/L. At this point the surgeon was unsure whether the patient was bleeding but queried a transfusion reaction. By this time the patient's circulation had shut down and she was transferred to ICU where a central line was inserted and fresh samples taken for referral and repeat Hb. Two hours later, and following a discussion between the blood service haematologist and the surgeon, it was agreed that uncrossmatched ABO/RhD identical red cells should be transfused. However, during these discussions the patient died.

The blood service reference laboratory later reported anti-c plus further unidentified reactions by IAT and a pan-reacting antibody at 16^{o}C. There was some indication of anti-c in the eluate. As a result of this incident, the laboratory is reviewing its antibody investigation and reporting mechanisms.

This case highlights several points:

- A need to recognise a DHTR at both laboratory and ward level
- A need to appreciate that phenotyping patients' red cells post transfusion may be of little value
- A need to involve the hospital haematologist earlier
- A need to understand limitations of in-house serological investigations and refer sooner

Analysis of serological information

Table 37 gives information on the techniques used for antibody screening in the 47 reported cases. An IAT crossmatch was performed in 35 cases, an immediate spin crossmatch in 5 cases and electronic issue in 5 cases. No pre-transfusion crossmatching was performed in 2 emergency cases.

Table 37
Techniques used for antibody screening and crossmatching

IAT screening technology	Number of cases
BioVue	17
DiaMed	20*
LISS tube	3
CRRS+DiaMed	2
LP microplate	1
Solid Screen	1
Scangel	1
None	2
All techniques	47

*In one case a CRRS screen was also performed and found to be positive

The IAT technology used for antibody screening broadly reflects that being used in the UK with approximately 82% of antibody screens in non-reference laboratories being performed using Column Agglutination Technology (DiaMed ID 54%, Ortho BioVue 28%) and 13% solid phase technology (data from UK National External Quality Assurance Scheme (NEQAS) questionnaire, February 2003).

In only 5 cases (11%) was there a report of an eluate being performed. In one case the anti-Jk^b was only detected in the eluate, highlighting the importance of this test when investigating suspected DHTRs.

In 24 (53%) cases the pre-transfusion sample was retested and the same result was obtained in 22 (92%) of them. This was reported as being confirmed by a reference laboratory in only two cases. The remaining reports did not state who repeated the testing or by what techniques. In two patients (cases 31 and 44, described below), a weak anti-Jk^a was missed by automated pre-transfusion testing but detected retrospectively using a manual technique.

In 34 cases (77%) plasma was used and in 10 cases serum (1 not stated and 2 no pre-transfusion testing performed). This appears to be a higher proportion of plasma samples than would be expected from the proportion of laboratories employing automated grouping and screening techniques. However, recent data obtained from a UK NEQAS questionnaire shows that approximately 86% of antibody screens undertaken in UK hospitals are performed using plasma rather than serum, reflecting the data presented in this report.

The post transfusion DAT was reported to be negative in 7 cases and was not performed in 4 cases.

Interval between drawing the crossmatch sample and transfusion

Table 38
Interval between drawing the crossmatch sample and transfusion

Interval between crossmatch and sampling (hrs)	No. cases
<48	33
48-71	1
72-96	1
>96	5
Not stated	5

As far as it is possible to tell from the questionnaire the vast majority of the samples were taken within the time limits recommended in the BCSH guidelines[13]. In one case described below (case 36) a 4-week old pre-assessment sample was used, despite the fact that the patient had received a very recent transfusion (probably unknown to the reporting hospital at the time). In a second patient, already described (case 7) a 48 hour old sample was used, following transfusion 5 days previously. In this case, BCSH guidelines would recommend a fresh sample, however, it was thought that the patient was bleeding and transfusion was presumably requested urgently.

Reporting to Blood Centres and Hospital Transfusion committees

A total of 26 (58%) incidents were reported to the local Blood Centre and 33 (73%) to the Hospital Transfusion Committee, with a further 5 indicating that they would report to a future meeting. Three respondents said that they had not reported to either and 2 did not answer the question.

Details of some of the interesting cases are given below:

Case 42
An 80 year old male patient, underwent emergency vascular surgery for an aortic aneurysm. No previous transfusion history was known. Pre-transfusion testing typed the patient as A RhD negative, antibody screen negative by DiaMed IAT (rapid/urgent technique) using plasma (DAT not performed). The patient was transfused with 28 units of A RhD negative red cells, followed by 12 units of A RhD positive (after depletion of local stocks of A RhD negative). Ten days post-transfusion, the patient's Hb fell and spherocytes were noted on the blood film. Post-transfusion serology revealed anti-D in the patient's plasma, but a DAT was not performed. The patient was already on ICU but required further red cell transfusions. He survived with no further ill effects. As a result of this incident there have been recommended changes in practice with respect to investigation of a suspected transfusion reaction, particularly performance of a DAT. Although there was no previous transfusion history known, it is impossible that this was due to a primary immune response.

In a similar case (case 3) a 75 year old, RhD negative, female patient (with an uncertain transfusion history but with previous pregnancies) was electively transfused with 2 units of RhD positive red cells. An unspecified number of days later her Hb fell and she became jaundiced. Her DAT was positive and anti-D was detected in her serum. She required admission and further transfusion.

Case 36
A 43 year old female patient with sickle cell disease was exchange transfused with 10 units of red cells prior to a total hip replacement on Day 1 (in hospital 1), followed by four units of red cells in theatre (in hospital 2) on Day 3. Pre-transfusion testing for the latter transfusion was performed using a sample taken at least three weeks earlier at a pre-assessment clinic in hospital 2. The antibody screen on the pre-assessment sample was positive by routine BioVue IAT and anti-E was identified by BioVue IAT. E negative blood was crossmatched for Day 3 by routine BioVue IAT on the stored plasma sample. On Day 10, the patient was admitted with dark urine, jaundice and a falling Hb (from 84g/L to 35g/L). This was initially assumed to be due to a sickle cell crisis and IvIg was prescribed. On Day 12 a sample was taken for serological testing. Anti-C+E+S+Jk^a+Fy^a were identified by the reference laboratory, plus a further unidentified antibody, but the DAT was negative. The patient required admission to the ward, folic acid, oxygen and further transfusion. She survived with no further ill effects.

This case highlights the potential problems associated with having care shared between hospitals. The patient was seen in outpatients by a visiting consultant with specialist interest in SCD, who recommended transfusion with Rh and K matched blood, however as an in-patient she was seen by the consultant from the host hospital and E negative blood only, was ordered by a junior doctor. It is implied that although the host hospital has a policy of transfusing Rh and K matched blood for patients with SCD, they were unaware that the patient had SCD. Although some details are unknown, it is clear that there was confusion and lack of communication between the hospitals, leading to an old sample being used for crossmatching and the protocol for selecting blood for transfusion to patients with SCD not being followed.

Case 38

A 27 year old female patient received red cells and plasma on ICU post splenectomy. The pre-transfusion screen was performed by manual DiaMed IAT simultaneously with the IAT crossmatch as it would have been too late to wait for the next automated Capture R batch. The screen was negative, the crossmatch was compatible and the blood transfused. Later that day, the antibody screen was found to be positive by the routine Capture R technique, but non-specific reactions were obtained and no further action was taken. New samples were taken and sent to the reference laboratory. Four days later a fresh sample was sent with a request for further crossmatching. The blood was found compatible by DiaMed, but the auto was positive and the antibody screen weakly positive. Simultaneous testing by an automated Capture R technique gave a positive screen. Anti-E was identified by DiaMed IAT and anti-c+E by DiaMed papain. Testing with Capture R revealed anti-c+E plus another unidentified specificity. The reference laboratory gave the results of the original pre-transfusion sample as anti-c+E+Jk^a (techniques not specified by the reporter). In-house retrospective testing of the pre-transfusion sample gave the same results as previously. The patient had no symptoms and survived with no ill effects.

This case raises questions about the investigation of positive antibody screens. When the initial Capture R screen was found to be positive, a DiaMed panel performed by an enzyme technique may have been helpful. An IAT using enzyme treated cells may also be considered when positive reactions fail to give a clear specificity.

Case 44

A 79 year old female patient received 7 units of blood for knee arthroplasty. The antibody screen was negative using a routine automated DiaMed technique and blood was compatible using an 'immediate spin' crossmatch. Another sample taken 14 days later revealed a positive DAT and anti-Jk^a in the plasma. Retrospective testing of the pre-transfusion sample by manual DiaMed testing revealed a weak positive antibody screen with the Jk(a+b-) screening cell, whilst automated testing was still negative. The patient had no symptoms of haemolysis and survived with no ill effects. As a consequence of this event, this laboratory started visually checking all cards processed by the automation and DiaMed were asked to increase the sensitivity of the camera.

Case 31

A 63 year old multi-transfused female patient with pre-existing anti-E received 2 units of E negative blood for melaena. The pre-transfusion screen and crossmatch were performed using an automated DiaMed technique. Two days later there was evidence of haemolysis with dark plasma and a falling Hb. A new sample revealed a positive DAT and anti-Jk^a in addition to the anti-E. Retrospective testing of the pre-transfusion sample revealed a weak anti-Jk^a reactive by manual DiaMed but not automated DiaMed.

COMMENTARY

- In two out of the three cases resulting in mortality, the delayed haemolytic transfusion reactions were overlooked and in one case, an incorrect assumption that the drop in haemoglobin was due to bleeding, led to an unnecessary further laparotomy.

- In two out of these three cases, there were critical delays in obtaining red cells for transfusion to correct the anaemias, which in turn led to cardiac decompensation.

- Kidd and/or c antibodies were implicated in approximately 75% of all cases, in over 90% of all patients in whom antibodies were found and 100% of deaths related to the transfusion.

- There were two cases of anti-D where elderly RhD negative patients (one female, one male) were transfused with RhD positive blood, one because of policy and the other because of an emergency. It is worth noting that RhD negative women whose pregnancies occurred before routine post-natal anti-D prophylaxis may have been previously sensitised to the D antigen.

- There is insufficient information from the questionnaires to be sure that sufficient investigation is being undertaken to investigate DTRs. Only 11% reported that a red cell eluate had been performed, 4 did not perform a DAT, and only 2 stated that the pre-transfusion sample had been tested retrospectively by a reference centre. Without detailed information about *how* retrospective testing was performed (where and by what techniques) it is impossible to know whether any of the implicated antibodies could or should have been detected pre-transfusion.

- There were 2 examples of Kidd antibodies that were missed pre-transfusion, only detectable (by the technique used) using red cells bearing homozygous (double-dose) expression of the relevant antigen.

- The 7 patients in whom the DAT was negative all fell into severity categories 3 and 4. Although an important part of the investigation of a DHTR, a negative result must not be regarded as conclusive lack of evidence for a DHTR.

- There is no evidence that laboratories are not following guidelines with respect to timing of samples in relation to the transfusion. There were only two cases, where an inappropriate sample was obviously used for pre-transfusion testing; in one case the laboratory were unaware of a recent transfusion and in the other case the transfusion was required urgently. The majority of DHTRs were evenly spread between 1 and 14 days following the implicated transfusion, confirming the need to follow the BCSH guidelines[13] with respect to sampling and previous transfusion.

RECOMMENDATIONS

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

- **If no antibody is detected in a case of suspected DHTR, more sensitive techniques should be considered, e.g. enzyme or enzyme antiglobulin techniques.**

- **Serum (+ plasma, if used routinely) should preferentially be used for investigation of suspected DHTRs, to give the maximum potential for identifying all specificities present, including weak complement binding antibodies.**

- **It is recommended that patients with SCD are phenotyped prior to transfusion and that blood is selected for Rh and K[13].**

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

- **Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies. These should be accompanied by patient information leaflets, explaining the significance of the antibody and impressing that the card should be shown in the event of a hospital admission or being crossmatched for surgery.**

- **When the care of patients with haematological disorders requiring transfusion support is shared, there is a risk that not all pertinent transfusion history will be available to both sites. In the absence of networked pathology information systems, it is essential that local procedures are devised for adequate communication between laboratories as well as clinical teams.**

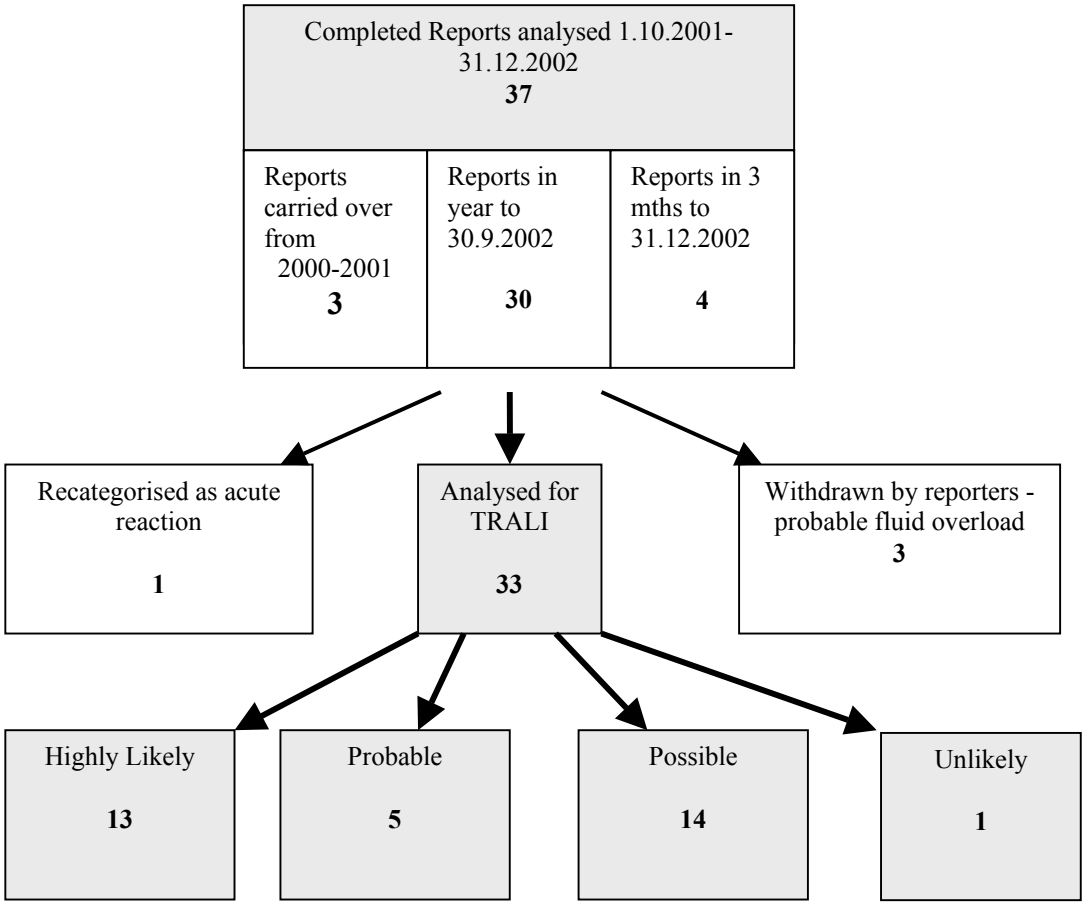
- **When the laboratory cannot supply compatible red cells within the time-frame requested, there should be communication between the haematologist and the responsible clinician to determine whether the risk of delaying the transfusion outweighs the risks of a transfusion reaction and whether potentially incompatible units should be given.**

14. TRANSFUSION-ASSOCIATED 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.

There was a large increase in the number of cases reported this year with a total of 33 completed reports, of which three were reports brought forward from last year, and four reports came between October and January i.e. the additional 3 months included this year. This leaves 26 new cases in the 12-month period 01/10/01 to 30/09/02, compared with 15 new cases in the corresponding period last year. In addition to the 33 completed reports, a further 4 reports were received of which three were subsequently felt by the reporters not to be due to TRALI and one was felt to be more appropriately included in the 'acute reaction to transfusion' category. These additional cases are not included in the analysis. Figure 26 summarises this information.

Figure 26
Summary of cases reported



TRALI can be a difficult diagnosis to make and difficult to distinguish from other causes of acute lung injury. If the symptoms and signs occur in a previously fit patient and there is positive serology for leucocyte antibodies, the diagnosis is straightforward. Very often however it occurs in a sick patient who has been given a considerable volume of fluid and may have other reasons to develop Acute Respiratory Distress Syndrome (ARDS).

Serology may also not be definitive. Because of the frequency of leucocyte antibodies in the donor population (5-10% of female donors), donor antibodies would be found in uneventful transfusions if they were similarly investigated. Because of this, the likelihood of a case being TRALI was assessed by two Consultants from the SHOT team (one of whom assessed the cases in previous years). The likelihood was graded on the basis of clinical features as reported to SHOT and the available serology. Serology was not available in 7 cases.

Cases were divided into 4 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.

A breakdown of the cases by age and gender is shown in figure 27 below. This shows that all age ranges are represented with a peak in the older age group in which transfusion is more common. The cases were also analysed by reason for transfusion as shown in figure 28. The previous preponderance of haematological cases has been overtaken by surgical cases, possibly as a result of increased awareness and recognition of TRALI in more complex clinical situations.

Figure 27
TRALI cases by age and gender

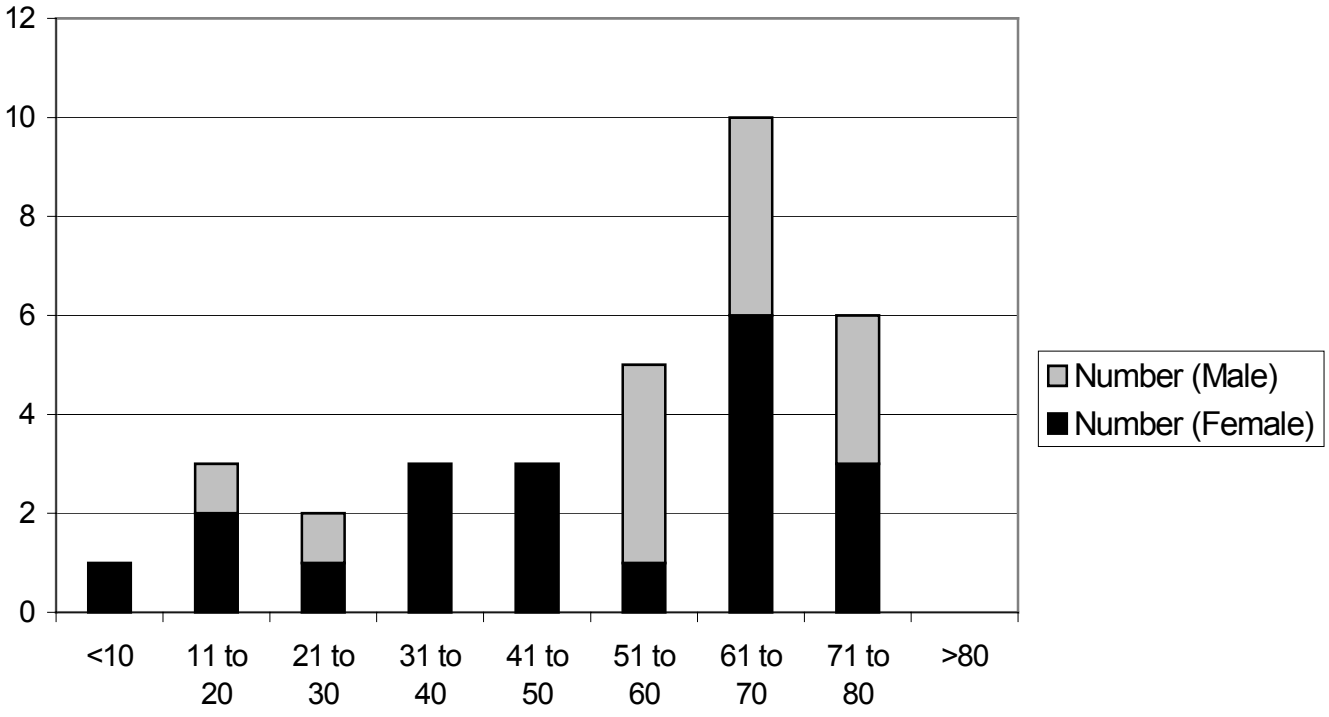
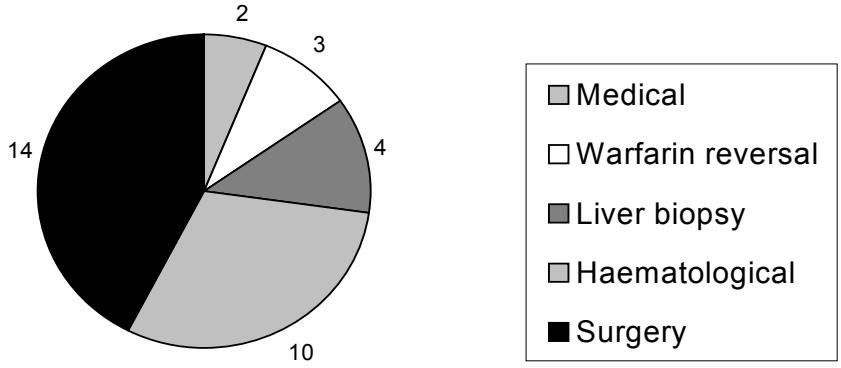
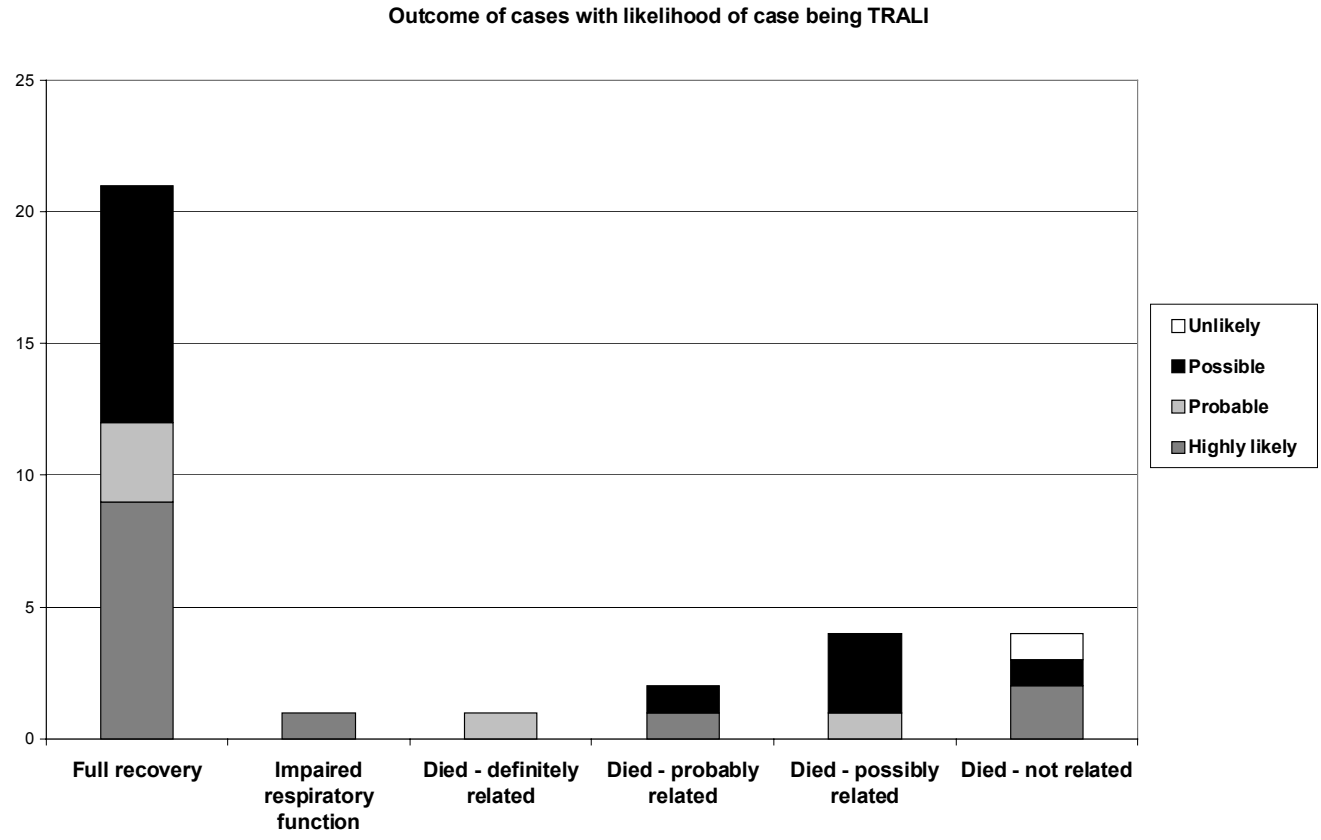


Figure 28
TRALI cases by indication for transfusion



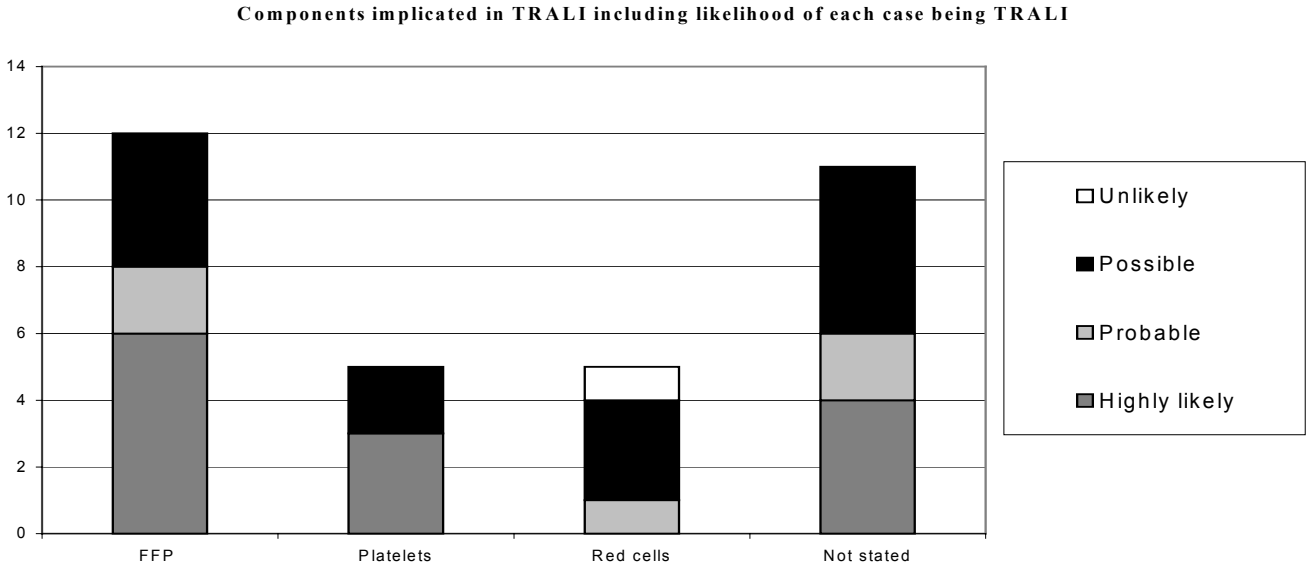
The majority of patients (21) subsequently made a full recovery (one patient was included in this category where it was not clear at the time of reporting whether the patient was going to make a full recovery or have some residual impairment). One patient was reported to have recovered but with impaired respiratory function. Overall 11 patients died see figure 29 below, of which 7 were at least possibly related to the transfusion. In the opinion of the reporters these were thought to be 'definitely due to transfusion' in 1 case, 'probably due to transfusion' in 2 cases, 'possibly due to transfusion' in 4 cases and 'unrelated to transfusion' in 4 cases.

Figure 29
Outcome based on reporter's assessment



The component most commonly associated with the development of TRALI was fresh frozen plasma (12 cases) with a combination of components in 11 cases, platelets alone in 5 cases and red cells in 5 cases. (Figure 30)

Figure 30
Components implicated in TRALI



Tables 39, 40, and 41 give a summary of the details of all cases as reported to SHOT. Three cases are described below. The first illustrates a classic example of TRALI. The second shows an example of a case where the diagnosis is more difficult and the third is of interest as involves a reaction to Octaplas pooled solvent detergent FFP

*Where cases were 'not stated' more than one product had been given

Case 1

Case 1 was a 47 year old lady with primary biliary cirrhosis admitted for a routine liver biopsy. She was given 4 units of FFP prior to the biopsy. During the 3rd unit she became dyspnoeic and tachypnoeic with a cough. Her blood pressure dropped from 130/85 to 105/60 and she became hypoxic with O_2 saturation of 63% on air and a PaO_2 of 8.8kPa on 70% oxygen. She was mildly pyrexial with a temperature of 37.5°C. Chest X ray showed 'severe pulmonary oedema' but her central venous pressure (CVP) was not raised. A subsequent echocardiogram showed no cardiac dysfunction and her electrocardiogram was normal. She was treated on the high dependency unit with oxygen via continuous positive airways pressure (CPAP). She made a full recovery. The patient and donors were investigated. The patient was not found to have anti-leucocyte antibodies. One of the four donors who was female and had had previous pregnancies was found to have an HLA class II antibody with anti-DR17 specificity. The patient was DR17 positive and the cross-match against patient's lymphocytes was weakly positive.

Case 2

Case 2 was a 31 year old woman who was being investigated for abdominal pain and jaundice of unknown aetiology. She was given 6 units of FFP prior to liver biopsy as her INR was 1.7. Her albumin was also low. Following the biopsy her blood pressure dropped to 100/50 and she was given a further 6 units of FFP. Her blood pressure dropped further to 60/29 and her oxygen saturations were 60% on air. She was given 500mL of

Haemocell. The patient was reported to be wheezy bilaterally with crackles. A chest X-Ray (CXR) showed 'pulmonary oedema' and consolidation at the left base. She was admitted to ICU, given CPAP and treated for fluid overload. By this stage, she had received over 3 litres of fluid, the majority of which was FFP. Antibody screening of the donor samples showed two donors to be positive for HLA antibodies, one weakly for IgM antibodies and the other for HLA class I. In the crossmatch, positive reactions were obtained in the case of the donor with HLA class I antibodies. Serology of the patient showed that she had anti-neutrophil antibodies. Overall the clinical picture in this case points much more to fluid overload than TRALI but illustrates that, in the face of the positive serology, it is difficult to exclude TRALI and this has been categorised as 'possible.'

Case 3

Case 3 was a 28 year old woman with pregnancy-associated thrombotic thrombocytopenic purpura. After delivery she was being treated as an outpatient with daily infusions of 4 units of FFP. She reacted to standard FFP with an urticarial rash and facial swelling and was therefore switched to Octaplas pooled solvent detergent FFP. She received 2 infusions with Octaplas pooled solvent detergent FFP without problems and then had a day off treatment. The following day she received her 3rd infusion of Octaplas pooled solvent detergent FFP this time from a different batch. Six hours later she became breathless at home and was admitted with severe shortness of breath on minimal exertion. Her BP was 150/109, pulse 111, temperature 37.2°C and percutaneous oxygen saturation was 92% on air. CXR showed diffuse alveolar shadowing consistent with ARDS or pulmonary oedema. She was treated with oxygen, diuretics and salbutamol nebulisers. She made a steady recovery with saturations of 98% on air the following morning. Her peak expiratory flow rate was 280 on admission and 300 the following morning. She subsequently received a further infusion of Octaplas pooled solvent detergent FFP from the same batch without untoward effects but this time she had diuretic and steroid cover. She had noticed a cough during her pregnancy which worsened with the 3rd bag of each infusion but had not previously been breathless. Subsequent investigations 3 months later showed no evidence of a cardiac problem with a normal echocardiogram. Both batches of Octaplas pooled solvent detergent FFP were tested. Tests for HLA class I and II antibodies were negative. The implicated batch showed weak borderline positive results with lymphocytes from 5 of 6 donors using the Glam assay. The other batch contained a weak lymphocyte reactive antibody.

This case, like case 2, illustrates some of the difficulties in making a diagnosis of TRALI in a complex clinical situation. It is possible that this represented a reaction to plasma proteins or possibly fluid overload but the timing and CXR appearance would fit with TRALI.

COMMENTARY

- TRALI remains a potentially serious consequence of transfusion. There was one patient whose death was considered to be 'definitely due to transfusion' and 2 others were 'probably due to the transfusion'.

- The number of cases reported this year has increased although in 2 cases the actual transfusion occurred in 2000 and 3 cases were reports received in this reporting period but initially reported last year. It would however suggest that clinicians are becoming more aware of TRALI.

- The cases illustrate the difficulty in establishing a diagnosis in a condition which is essentially a diagnosis of exclusion. Serology is helpful but about 8% of female donors will have leucocyte antibodies and their presence in an implicated donor does not necessarily mean that they were interactive with the patient. It is important to investigate these cases by referring them to the blood service laboratories and where possible to do a patient/donor 'crossmatch'. As a minimum, the patient should be shown to possess the corresponding antigen.

- The first 2 cases highlight the potential dangers of using FFP routinely to attempt to correct an elevated INR in patients undergoing liver biopsy. In case 1, reporters have said that in light of this case they will review their policy on the use of FFP for liver biopsies in patients with a prolonged PT and consider using the transjugular route instead.

RECOMMENDATIONS

- **Hospitals should continue to be aware of TRALI and to investigate and report possible cases. Continued education of all staff about this condition is encouraged so that cases may be investigated appropriately and implicated donors withdrawn.**

- **The analysis was unsatisfactory as many cases were not fully investigated and clinical details were sketchy. It is recommended that there is early evaluation of cases by the consultant(s) involved. A team approach including the haematologist and chest physician and/or ICU consultant may be helpful. The blood services are refining the algorithm for investigation of TRALI so the laboratory investigation of cases should be more consistent and complete.**

- **FFP continues to be associated with significant risks of reactions including TRALI and should only be used when clinically indicated in accordance with BCSH guidelines[8]. It is particularly important that guidelines for the management of high INRs due to warfarin therapy are also followed[9].**

- **UK Transfusion Services should take all steps possible to reduce the risk of TRALI from blood components especially FFP and platelets.**

Table 39 UNDERLYING DIAGNOSIS AND TRANSFUSION HISTORY OF PATIENTS REPORTED AS TRALI

TRALI Case No.	Age/sex	Diagnosis	Reason transfused	*Components transfused*			Incriminated component	Interval between commencement of transfusion and symptoms
				RBC	Plt	FFP		
1	F/69	AML	Low platelets		2		Platelets	10 mins into 2nd unit
2	F/62		GI bleed	14	1	6	Not stated	Within 24 hours
3	F/38	Jaundice/ hepatitis	Liver biopsy			4	FFP	2 hours after 3rd unit
4	F/59	AV replacement	Warfarin reversal because of high INR			3	FFP	2 hours
5	M/54	AML encephalitis post BMT	For line insertion		1		Platelets	30 mins
6	M/69	Ischaemic heart disease	Bleeding post CABG surgery		4		Platelets	15 - 30 mins
7	F/43	Caesarean - hysterectomy - placenta previa	Bleeding post hysterectomy	7		2	Not stated	Immediate
8	F/28	Pregnancy associated TTP	TTP			4 (Octoplas)	Octoplas	4 - 6 hours

Table 39 UNDERLYING DIAGNOSIS AND TRANSFUSION HISTORY OF PATIENTS REPORTED AS TRALI

TRALI Case No.	Age/sex	Diagnosis	Reason transfused	*Components transfused*			Incriminated component	Interval between commencement of transfusion and symptoms
				RBC	Plt	FFP		
9	F/59	Congenital heart disease	Replacement of R ventricular conduit	1		2	Not stated	2 hours
10	M/72	AIHA	Anaemia	4			Red cells	24 hours
11	F/47	Primary biliary cirrhosis	Liver biopsy			4	FFP	During 3rd unit
12	F/73	Fractured neck of femur; AF on warfarin	Warfarin reversal			3	FFP	1 hour
13	F/65	Breast lump	Mastectomy	8		6	Not stated	2 days
14	F/73	Myelodysplastic syndrome	Low platelets		1		Platelets	30 mins
15	M/61	Abdominal aortic aneurysm repair	GI bleed, hypotensive with Hb 4.2 g/dl	2			Red cells	During transfusion
16	F/71	Cryptogenic cirrhosis	Gastroscopy and paracentesis, PT 22 seconds			3	FFP	During 3rd unit
17	F/31	Chronic hepatitis	Liver biopsy			6 + 6	FFP	After 6th unit

Table 39 UNDERLYING DIAGNOSIS AND TRANSFUSION HISTORY OF PATIENTS REPORTED AS TRALI

TRALI Case No.	Age/sex	Diagnosis	Reason transfused	*Components transfused*			Incriminated component	Interval between commencement of transfusion and symptoms
				RBC	Plt	FFP		
18	F/35	Menorrhagia	Laparotomy for bleeding after elective hysterectomy	11	1	3	Not stated	20 hours after 1st unit
19	F/67	MVD on warfarin	GI bleed, high INR	5		6	Not stated	Not stated
20	F/41	AML – M3	Not stated – presumed DIC		3	3 FFP and 10 cryo	Not stated	4 - 6 hours
21	F/18	Fractures		1			Red cells	1 hour
22	M/60	Prostate cancer	Haemorrhage during radical prostatectomy	4		4	Not stated	2.5 hours
23	F/64	ITP and AIHA	Low platelets on CAMPATH		1		Platelets	Not stated
24	M/80	Myocardial infarction/streptococcal infection	Not stated	2			Red cells	6 hours
25	M/79	Coronary artery disease	CABG	3	1	3	Not stated	2 hours

Table 39 UNDERLYING DIAGNOSIS AND TRANSFUSION HISTORY OF PATIENTS REPORTED AS TRALI

TRALI Case No.	Age/sex	Diagnosis	Reason transfused	*Components transfused*			Incriminated component	Interval between commencement of transfusion and symptoms
				RBC	Plt	FFP		
26	F/19	Caesarean section	Anaemic 3 days post-operation	2			Red cells	Within 4 hours
27	M/22	AML - M5	Not stated		1	4	FFP	During 4th unit of FFP
28	M/61	Ischaemic heart disease	CABG x 3	1		3	FFP	After 3rd unit of FFP
29	M/53	NHL 2 months post autograph	Not stated		1	1	Not stated	Soon after transfusion
30	M/51	Atrial septal defect	Haemorrhage due to surgery to close ASD			4	FFP	End of 4th unit
31	M/18	Cancer	Thoracotomy for metastasectomy			4	FFP	Not stated
32	M/62	Coronary artery disease	CABG			3	FFP	Immediately post transfusion
33	F/64	Myeloma	Not stated	2	1		Not stated	8 hours

Table 40 **CLINICAL AND RADIOLOGICAL FEATURES OF CASES REPORTED AS TRALI**

TRALI Case No.	Risk Factors	Symptoms/Signs						
		Fever or rigors	Hypotension	Dyspnoea/ Tachynoea	PAWP	pO2kPa	Echo	CXR
1	ATRA		N	Y		5.4		Bilateral interstitial shadowing
2	CCF, sepsis, shock, low albumin	Y	Y		Low	Low		Diffuse interstitial infiltrates
3	No		Y (80 syst)	Y		8.8 (air)	Good LV function	Bilateral alveolar shadowing, lower and mid zones
4	Albumin 30 g/l	N	N	Y		6.5		Not stated
5	Sepsis, aspiration, radiation to chest	Y	Y	Y		Low		Widespread consolidation, exacerbation of existing changes
6	Opiate analgesia, oxygen therapy	Y	Y (70/40)	Ventilated		6.1		Bilateral patchy infiltrates and atelectasis
7		Y		Y		5.5		Not stated
8	TTP, daily plasma	Y	N	Y + cough		Oxygen saturation 92%	Normal 3/12 later	Diffuse alveolar shadowing ARDS or pulmonary oedema
9	Recent upper respiratory tract infection		Y (35 syst)	Y + cough/sputum	Normal	4.5	Normal	Fluffy perihilar opacities

Table 40 **CLINICAL AND RADIOLOGICAL FEATURES OF CASES REPORTED AS TRALI**

TRALI Case No.	Risk Factors	Symptoms/Signs						
		Fever or rigors	Hypotension	Dyspnoea/ Tachynoea	PAWP	pO2kPa	Echo	CXR
10				Y		Oxygen saturation 70%		Picture of ARDS
11		Y	Y (105/60)	Y + cough	CVP not raised	8.8 on 70% oxygen	Normal	Severe pulmonary oedema
12	Ischaemic heart disease, COPD	Y	N	Y		8.4		Bilateral reticulonodular shadowing
13			Y	Cough		Not stated		Not stated
14		Y		Y		7		Possible bilateral basal parenchymal infiltration – subtle
15	Possible aspiration after gastroscopy	Y	Y	Y		4.2		Bilateral progressive alveolar consolidation
16	Low albumin, bilateral pleural effusions		Y	Y + cough + sputum		6.25	Good LV function	Characteristic appearances of ARDS/TRALI

Table 40 CLINICAL AND RADIOLOGICAL FEATURES OF CASES REPORTED AS TRALI

TRALI Case No.	Risk Factors	Symptoms/Signs						
		Fever or rigors	Hypotension	Dyspnoea/ Tachynoea	PAWP	pO2kPa	Echo	CXR
17	Low albumin		Y	Not stated		Low		Pulmonary oedema; consolidation L base; congestion R
18	Hypotension due to blood loss		Y	Y + cough		Low		Bilateral nodular shadowing
19			Y	Y		10.2 on oxygen		Bilateral airspace shadowing
20	ATRA	Y		Y + cough		8.4 on 35% oxygen		Bilateral basal infiltrates and perihilar shadowing
21	Multiple fractures	Y	Y	Y + cough	Normal	Low		Not stated
22		Y	Y (78/42)	Y	Normal	4.1		Not stated
23		Y	Y	Y		5.84		Bilateral interstitial infiltrates
24		Not stated	Not stated	Y		Not stated		Not stated
25		N	Y	Ventilated	Normal	9.2 (on 100% oxygen)		Bilateral lung shadows
26	Asthma, pre-eclampsia	Y		Y + cough		Low	Normal	Bilateral infiltrates esp. middle and lower lobes

Table 40 CLINICAL AND RADIOLOGICAL FEATURES OF CASES REPORTED AS TRALI

TRALI Case No.	Risk Factors	Symptoms/Signs						
		Fever or rigors	Hypotension	Dyspnoea/ Tachynoea	PAWP	pO2kPa	Echo	CXR
27		N	N	Y		5		Not stated
28	Ventilated post CABG	Y	Y (70/40)	Ventilated		Oxygen saturation 60%		White patches on CXR 'pulmonary oedema' cleared within 24 hours
29	Previous presumed fungal chest infection, radiation, granulocyte transfusion etc	Y	Y (60 syst)	Y		Low		Profound bilateral infiltrates (normal 5 hours before)
30	Four units FFP given earlier in the day	Y	Y	Y		Low		Slight consolidation for 24 hours
31				Y		7.8 on 60% oxygen		Bilateral pulmonary infiltrates
32	Ventilated post CABG	Y	Y			Low		Consolidation for 24 hours
33		Y	Y	Y		Low		Pulmonary oedema

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
1	Oxygen, hydrocortisone, nebulisers	HDU	N	Died-'not related to transfusion'	5 donors; 3 females tested; 1 HLA antibodies (A24, B7, B8): 1 non-specific granulocyte antibodies	Negative - patient HLA A24 and B7	Not performed - patient died	Timing, Xray changes and serology	Highly likely
2	Oxygen, methylprednisolone protease inhibitors, diuretics, fluids	Y	Y	Died-'possibly related to transfusion'	Donors tested, 2 negative, 3 weak ANA not clinically significant, 1 moderate HLA class II, 1 non-specific granulocyte antibody		Not performed - patient died	Acute decompensation, low wedge pressure	Possible
3	Oxygen, hydrocortisone	Y	N	Full recovery	4 donors investigated, 1 donor had lymphocyte and neutrophil reactive antibodies	Weak lymphocyte reactive antibody by GLAM assay		No pre-existing cardiac disease, normal echo, volume infused small	Probable

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
4	Hydrocortisone, oxygen, diuretics	N	N	Full recovery	Not performed	Not performed		Temporal relationship of FFP and dyspnoea	Possible
5	Oxygen, fluids, hydrocortisone, piriton	Already	Not stated	Died - 'not related to transfusion'	Negative	Weak lymphocyte reactive antibody either patient antibodies or from transfused unit	N	Complex situation but weak antibody in patient's serum	Possible
6	Oxygen, hydrocortisone, aprotinin, diuretics, fluids, intra aortic balloon pump	Y	Y	Died - 'possibly related to transfusion'	3 donors had possible granulocyte-reactive antibodies. One of these also had lymphocyte reactive antibodies. No HLA class I antibodies were detected			Temporal relationship to platelets – post mortem CCF++ no graft occlusion	Possible

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
7	Oxygen, diuretics	Y	N	Full recovery	1 of 6 Jersey donors had HNA-3a	Not stated - 10 pregnancies	N	Condition worse than expected for overtransfusion, much better next day	Possible
8	Oxygen, diuretics, ventolin nebulisers	N	N	Full recovery	No granulocyte antibodies, weak glam assay; HLA negative (Leeds)	HLA A23 and B15 detected 5 months later	Not reported	Felt on balance to be antibody mediated rather than overload but did receive further infusion of same batch under steroid cover with no ill effects	Possible
9	Oxygen, 19 hours on bypass, methylprednisolone	Y	Y (7 days)	Recovered ?full/ ?impaired respiratory function	The serum of 1 donor contained HLA class I (anti A2) and class II antibodies (anti-DR4 OR DQ8)	Patient HLA A2 and DR4. No leucocyte antibodies		Pulmonary oedema had albumin ++ consistent with lung injury, normal cardiac function	Highly likely

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
10	Oxygen, methylprednisolone diuretics, antibiotics	Y	Y (5 days)	Died 'not related to transfusion'	None had HLA or granulocyte antibodies	Negative for HLA/gran antibodies		Temporal relation to red cell transfusion, CVP did not suggest fluid overload; acute change in CXR 24 hours after transfusion	Unlikely
11	Oxygen, frusemide	HDU	CPAP	Full recovery	1 female donor has HLA class II anti-DR17 – patient DR17	No leucocyte antibodies	Weak positive with patients lymphocytes v implicated donor	ARDS not overload, time course fits	Highly likely
12	Oxygen, diuretics, hydrocortisone, piriton	HDU	N	Died 'not related to transfusion'	1 male donor not investigated; female donor HLA class I	Negative	Positive	Temporally related to 2 unit FFP although had previous IV fluids	Highly likely

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
13	Oxygen, methylprednisolone fluids	Already		Full recovery	3 males donors not investigated. 2/6 remaining donors were positive. One had non-specific HLA class I and one had granulocyte specific IgM Ab's	Negative	Both donors gave positive crossmatch reactions	Serology suggested TRALI likely	Possible
14	Oxygen, hydrocortisone, piriton, fluids	N	N	Full recovery	HLA class II antibodies detected in serum of donor who contributed plasma to platelet pool. Specificities DR4 and DR7	Negative	Positive	Acute onset of breathlessness during platelet transfusion resolving after 24 hours without diuretics	Highly likely
15	Oxygen	Y	Y (10 days)	Died - 'probably related to transfusion	Not available	Not available			Possible

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
16	Oxygen, hydrocortisone, frusemide, fluids, CPAP	Y	Y (7 days)	Died - 'definitely related to transfusion'	Awaited			Occurred during FFP, no response to diuretics, no other cause for ARDS, CVP not raised	Probable
17	Oxygen, methylprednisolone diuretics, fluids	Y	CPAP	Full recovery	2 untransfused males not tested; 2 donors HLA antibodies, one IgM, one class I	Positive for granulocyte antibodies	Positive for donor with class I antibodies	TRALI needs to be investigated as patient received 12 units FFP	Possible
18	Oxygen, fluids	Y	Y (4 days)	Full recovery	No granulocyte specific antibodies, one donor has possible HLA antibodies	Negative		Picture of ARDS, patient young; no prolonged hypotension	Possible
19	Oxygen, hydrocortisone, diuretics	Y		Full recovery	Both donors investigated. One had HLA antibodies; one HNA 1a	HLA antibodies	Positive with samples from both donors	Clinically LVF more likely	Probable

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
20	Oxygen, dexamethasone	N	CPAP	Recovery with impaired respiratory function	13 donors, 5 males not tested; 1 had granulocyte Ab, 1 has HLA class II	Negative	Positive with donor with ANA	Temporal relationship, possible ATRA syndrome but not characteristic	Highly likely
21	Oxygen, diuretics, fluids	Y	Y (19 days)	Full recovery	Negative	Negative		Temporal relationship, normal pulmonary CVP	Possible
22	Oxygen, diuretics, fluids	Y	Y (4 days)	Full recovery	1 donor antibodies to HLA DR1 – donor homozygous DR1	Not stated		Sudden onset without evidence of other cause, pulmonary artery wedge pressure consistent with non-cardiogenic pulmonary	High likely
23	Oxygen, hydrocortisone, fluids	Y	Y (3 days)	Full recovery	2 male donors not tested. 1 of 2 female donors positive for anti HLA-A11 and DQ2 + non specific	Negative (HLA A11 and DQ2 negative)	Positive		Highly likely

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
24	Not stated	Not stated	Not stated	Full recovery	Donor found to have 'neutrophil reactive antibody'		Positive	Clinical picture 'pulmonary oedema'	Possible
25	Oxygen, diuretics, fluids, hydrocortisone	Y (post op)	Y (4 days)	Died 'probably related to transfusion'	1/7 donors not investigated as untransfused male. Granulocyte specific antibodies detected in two	Negative	Not performed - patient died	Normal PAWP, abnormal CXR	Highly likely
26	Oxygen, diuretics	Y	Not stated	Full recovery	Not stated	Negative		Only received 300mL iv fluids, normal echo, CXR typical	Probable
27	Oxygen, diuretics, salbutamol	N	N	Full recovery	Untransfused male donors not investigated. Remaining donors negative	Negative		Onset clearly related to FFP infusion, no other recognisable cause of ARDS	Possible

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
28	Oxygen increased, noradrenalin, hydrocortisone, piriton	Already	Yes (2 days)	Full recovery	1 donor pos for HLA class II (DR14); one class I (A11). Patient DR14 and A11	Negative		Patient underfilled; CXR appearances resolved within 24 hours	Highly likely
29	Oxygen, methylprednisolone fluids	Y	Y (1 day)	Died - 'possibly related to transfusion' (+ severe sepsis)	Untransfused male donors not investigated. 1/3 female donors has HLA class I and II (no specificity)	Positive for granulocyte antibodies	Not done as patient died	No pulmonary signs/symptoms pre transfusion and normal CXR. ARDS a possibility in view of underlying sepsis	Probable
30	Oxygen, methylprednisolone	Already	Y - increased	Full recovery	1 donor had HLA antibodies with specificity DR1 plus non specific HLA. Patient DR1 negative	Negative	Positive	Sudden respiratory distress after FFP. Overload not suspected, filling pressures not high	Highly likely

Table 41 TREATMENT, OUTCOME AND DONOR SEROLOGY

TRALI Case No.	Treatment				Serology			Why did reporter think the case was TRALI rather than ARDS or fluid overload	Likelihood of case being TRALI
	Treatment	ITU	Ventilation	Outcome	Donors	Patient	Crossmatch		
31	Oxygen increased to 60%	Already	CPAP	Full recovery	2 male donors not tested; 2 females: 1 HNA 1a (patient HNA1a positive); 1 granulocyte spec Ab	Negative	Both positive	Pulmonary infiltrates developed in association with transfusion of FFP	Highly likely
32	Oxygen, noradrenalin	Already	Y - increased	Full recovery	1 male donor not tested; 2 females: 1 HLA class II (dr52) plus non specific HLA. Patient DR52 positive	Granulocytes spec autoantibodies	Positive cross match with donor with HLA antibodies	No indication of overload - dramatic response post transfusion	Highly likely
33	Not stated			Died - 'possibly related to transfusion'	Not available			Timescale	Possible

15. 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.

Four cases were reported as possible PTP. One case was excluded from analysis as the platelet count was low before transfusion and no HPA antibodies were detected. One case (case 1) had clinical features consistent with PTP but negative serology. The remaining 2 cases (cases 2 and 3) had classic features of PTP and in both cases the patient's serum was found to contain anti-HPA-1a.

Case 1

An 81 year old lady was admitted as an emergency with a fractured neck of femur. She had had no previous transfusions but had been pregnant in the past. She was given 2 units of red cells and about a week later she developed minor bleeding including haemoptysis. Her initial platelet count prior to transfusion was 259 x 10^9/L. This fell to a nadir of 28 x 10^9/L six days after transfusion and recovered spontaneously to > 50 x10^9/L five days later. HPA antibodies were not detected although the assay for anti-Gov (HPA-15) had not been established in the testing laboratory so their presence could not be excluded.

Case 2

A 35 year old lady with spina-bifida was admitted for cystoplasty. She had had one pregnancy and had been transfused as a child. She received 5 units of red cells and within a week developed purpura/bruising and minor haemorrhage. Her platelet count pre-transfusion was 203 x 10^9/L and fell to < 1 x 10^9/L nine days later. She was treated with high dose intravenous immunoglobulin and both random and HPA-1a negative platelets and her platelet count gradually rose to reach > 50 x 10^9/L two weeks later. Her serum was found to contain anti-HPA-1a.

Case 3

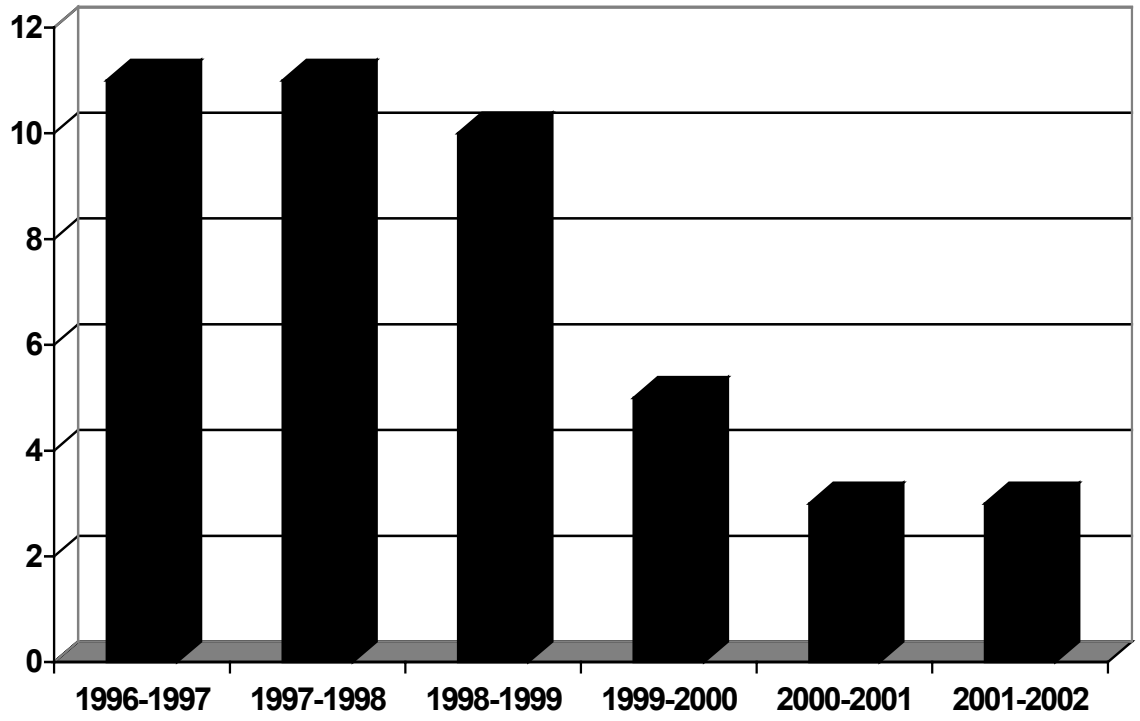
An 81 year old lady was admitted as an emergency with an upper gastrointestinal bleed. She received 15 units of blood and 2 units of FFP over a 9-day period. Nine days after the first transfusion her platelet count had fallen from a pre-transfusion count of 167 x 10^9/L to 5 x 10^9/L. She was treated with high dose intravenous immunoglobulin and random platelets and recovered to a platelet count of >50 x 10^9/L two days later. Serological investigations confirmed the presence of anti-HPA-1a.

COMMENTARY

- This year there were only three cases with a clinical history of PTP and in two the diagnosis was confirmed by positive serology. The graph below shows the number of PTP cases reported to SHOT each year since its inception in 1996. The reduction in the number of cases of PTP following the introduction of universal leucodepletion in 1998 is maintained. There does not appear to be significant under-reporting of known cases. From a telephone survey of the three NBS platelet immunology laboratories (by the analyst) the number of cases reported to SHOT is similar to the number of confirmed cases known to the laboratories. Other cases may of course occur but are not diagnosed as the patient does not have symptoms/signs. It is also possible for cases to occur following platelet transfusion but these are difficult to distinguish from platelet refractoriness and so are unlikely to be reported to SHOT.

Figure 31

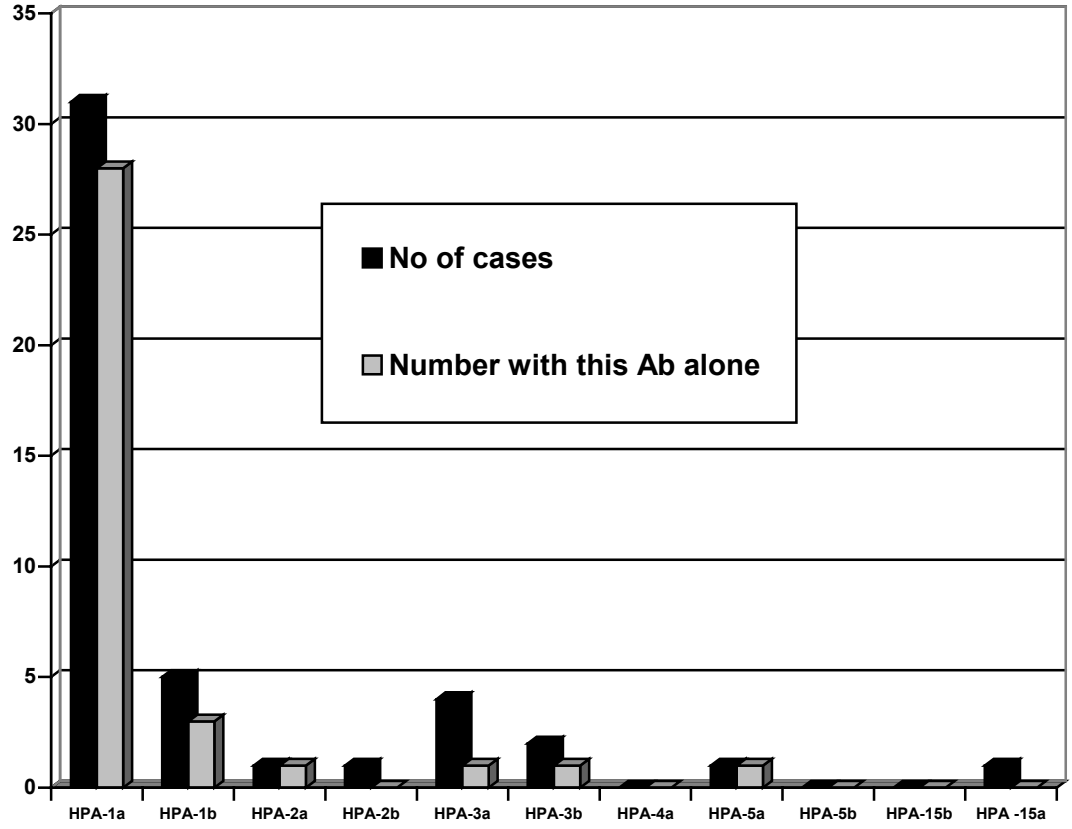
Number of cases of PTP reported to SHOT each year



- As in previous years the most common causative antibody remains anti-HPA-1a. The following graph illustrates the cumulative number of each antibody specificity associated with the PTP cases reported to SHOT. Detection of anti-HPA-15 (Gov) is in the process of being introduced in NBS platelet immunology reference laboratories. HPA-15 antibodies can be associated with refractoriness, neonatal alloimmune thrombocytopenia and PTP. Clinically suspicious cases with no detectable antibody will continue to be included as they may be due to other, as yet uncharacterised systems.

Figure 32

Antibodies associated with the PTP cases reported to SHOT



NB

Laboratories do not screen for HPA-4b, HPA-15a and HPA-15b were formerly known as Gov (b) and Gov (a)

RECOMMENDATIONS

- **Clinicians should remain aware of this rare but treatable consequence of transfusion. The treatment remains use of high dose intravenous gammaglobulins +/- steroids, with random (i.e. unmatched) blood components given only if there is significant bleeding.**

- **If PTP is suspected, there should be urgent liaison with a reference laboratory for appropriate specialist investigation**

- **PTP is induced by a re-exposure to HPA antigen in individuals with a history of previous immunising events. PTP can therefore occur following transfusion with any platelet-containing product. Now that leucodepletion removes most platelets from red cell components it may be that the classic picture of PTP occurring after red cell transfusion will change and we will see proportionately more cases following platelet transfusion. Non-classical cases should be reported to SHOT.**

- **Patients with HPA antibodies should have appropriate antigen-negative cellular products if they require transfusion in the future. Screening should be offered to female relatives of child-bearing potential to see if they are at risk of forming antibodies capable of causing fetal/neonatal alloimmune thrombocytopenia. For HPA-1a this would include HLA typing for HLA DR 101 to identify those who are likely to form antibodies.**

16. TRANSFUSION-ASSOCIATED GRAFT-VERSUS-HOST DISEASE

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

There were no new cases during this reporting period.

COMMENTARY

It is striking that, for the first 3 SHOT reports, 4 cases of TA-GVHD were reported each year, none of which was due to a failure to follow existing guidelines for the irradiation of blood products. Five cases occurred in patients with B cell malignancies who do not require irradiated products according to existing guidelines; 2 occurred in patients who were not known to be immunocompromised at the time of transfusion; and 5 occurred in apparently immunocompetant patients. In these patients there may have been partial haplotype sharing between the patient and a homozygous donor although this was only proven in one case.

In the subsequent 3 years only one case has been reported which was in a patient with B-acute lymphocytic leukemia (ALL).

Numbers are small but might imply that quality controlled leucodepletion of all blood components introduced by the UK Blood Services in 1999 may be partially protective, especially in reducing the risk of TA-GVHD in immunocompetent patients.

Table 42 gives and updated summary of all the cases of TA-GVHD reported to SHOT.

Table 42
All cases of TA-GVHD reported to SHOT 1996 - 2001

Year	No cases	Diagnoses	Shared haplotype	Outcome
1996-97	4	• Congenital immunodeficiency • No risk factors • B cell NHL • B cell NHL	Yes NK NK NK	Died Died Died Died
1997-98	4	• Waldenstrom's macroglobulinaemia • B cell NHL • Cardiac surgery • ITP	NK* Yes Yes NK	Died Died Died Died
1998-99	4	• Myeloma • Uncharacterised immunodeficiency • Cardiac surgery • Cardiac surgery	NK NK NK Yes	Died Died Died Died
1999-00	0			
2000-01	1	• B ALL	NK	Died
2001-02	0			

* donor homozygous

RECOMMENDATIONS

TA-GVHD remains a fatal consequence of transfusion.

- **Despite the lack of cases this year, hospitals should remain aware of the condition and should be rigorous in putting systems in place to ensure that all patients at risk of TA-GVHD receive gamma irradiated products. Once again this relies crucially on good communication, especially when a patient's care is shared between hospitals. Clear protocols need to be in place to ensure that information is passed on. Measures such as the use of the BCSH/NBS patient card and leaflet 'Information for patients needing irradiated blood' are also recommended.**

- **Products where partial haplotye sharing is likely should be irradiated. If donor lymphocytes are homozygous for one of the patient's haplotypes the donor lymphocytes can survive. Because they do not share the other haplotype of the patient, however, they can recognise the patient as foreign and set up a GVHD reaction. This is particularly likely to happen if HLA matched products or products from family members are used and for this reason these products should always be irradiated.**

- **New chemo- or immuno- therapeutic regimes should be assessed for their potential to cause TA-GVHD and guidelines modified accordingly.**

17. TRANSFUSION-TRANSMITTED INFECTIONS

Definition
A post-transfusion infection was classified as a transfusion-transmitted infection if the following criteria were met at the end of the investigation: -

- the recipient had evidence of infection post-transfusion, and there was no evidence of infection prior to transfusion

and, either

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

or

- at least one component received by the infected recipient was shown to have been contaminated with the agent of infection

Introduction

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in a particular year can therefore accrue over the subsequent year(s). The number of cases ascertained by the end of any period is therefore expected to be an incomplete picture of the infections transmitted during that period. The reporting of acute infections, such as bacteraemias, that tend to be clinically apparent and diagnosed within days after receipt of the infectious transfusion, may be relatively complete but chronic viral infections will be underrepresented.
In addition, the occurrence of disease, or the observation of serological markers of infection, in individuals who have donated blood can lead to the ascertainment of transfusion-transmitted infections by tracing and testing of recipients exposed to components collected from donors during potentially infectious periods. Recipients may be asymptomatic at this time and only identified by this investigation.

Post-transfusion infections may be due to an infected (or contaminated) transfusion or infection that may have been acquired from another source. Investigation of markers of infection in an implicated donation, or in subsequent samples from the donors of implicated donations, can confirm transfusion as the probable cause of infection, or identify the need to investigate other possible sources. The blood service must therefore be informed about implicated transfusions so that investigations can be conducted to confirm or refute the suspicion that the implicated transfusion(s) may have been infectious. This is essential to prevent further transmission(s) by other components and/or by chronically infected donors, and to reveal any systematic errors or deficiencies in the blood service testing. Such investigations may involve microbiological testing of many donors and may take several months to complete.

A surveillance system to collect standardised information about infections suspected to have been transmitted by transfusion was introduced in the UK (excluding Scotland) and the Republic of Ireland by the National Blood Authority and the Health Protection Agency Communicable Disease Surveillance Centre in October 1995. Reported data from England, Wales and Northern Ireland are included in this report.

A similar collation of reports of cases investigated by Scottish blood centres has been in place in Scotland since October 1998.

Methods

Participating blood centres in England, Wales and Northern Ireland reported all post-transfusion infections of which they had been informed to the NBS/Health Protection Agency Infection Surveillance. The criteria for identifying infections eligible for reporting as post-transfusion infections were either:

a) the receipt of the transfusion had been confirmed and the infection in the recipient had been confirmed (by detection of antibody, antigen, RNA/Deoxyribonucleic acid or culture) and there was no evidence that the recipient was infected prior to transfusion, (see exception below) or,

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

and c) the case did not involve HCV or HIV infections diagnosed in recipients who had received transfusions in the UK that were not tested for anti-HCV (i.e. pre September 1991) or anti-HIV (i.e. pre October 1985) respectively. (These cases have been excluded because the blood service is rarely able to conduct follow-up investigation of all donors implicated and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions.)

and d) the case did not involve human T-cell leukaemia virus (HTLV) infections diagnosed in recipients who had received transfusions in the UK prior to August 2002 when screening for anti-HTLV was first implemented. As a result of screening the NBS has begun a national 'lookback' programme to identify any recipients of blood donated by anti-HTLV positive donors before the introduction of testing. Any post-transfusion HTLV infections identified through the 'lookback' are excluded from this report (see c above) but will be reported to the NBS and analysed and published elsewhere, as was done previously with HCV 'lookback'.

If other possible sources of infection were known for a post-transfusion infection, an initial report was still requested.

Information about the recipient, the recipient's infection and the transfusion(s) implicated as the possible source of infection formed the basis of the initial report. Subsequently, after appropriate investigations had been completed, details about the findings of the investigation were reported. (PTI report forms are in appendix 5)

Data received by 31/3/2003 about incidents of transfusion-transmitted infections initially reported by blood centres between 01/10/2001 and 31/12/2002 are included in this report. Data received about incidents reported during the previous six years of the surveillance system are included in a cumulative table (table 43).

Unless the investigation was closed due to the identification of a probable source of infection other than transfusion, investigations that were closed without being able to conclusively investigate the source of the post-transfusion infections were classified as post-transfusion infections of undetermined source.

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

Results

Between 01/10/2001 and 31/12/2002, 34 post-transfusion infections were reported by blood centres in the UK, 28 from blood centres in England, Wales and Northern Ireland and 6 from Scotland (figure 33).

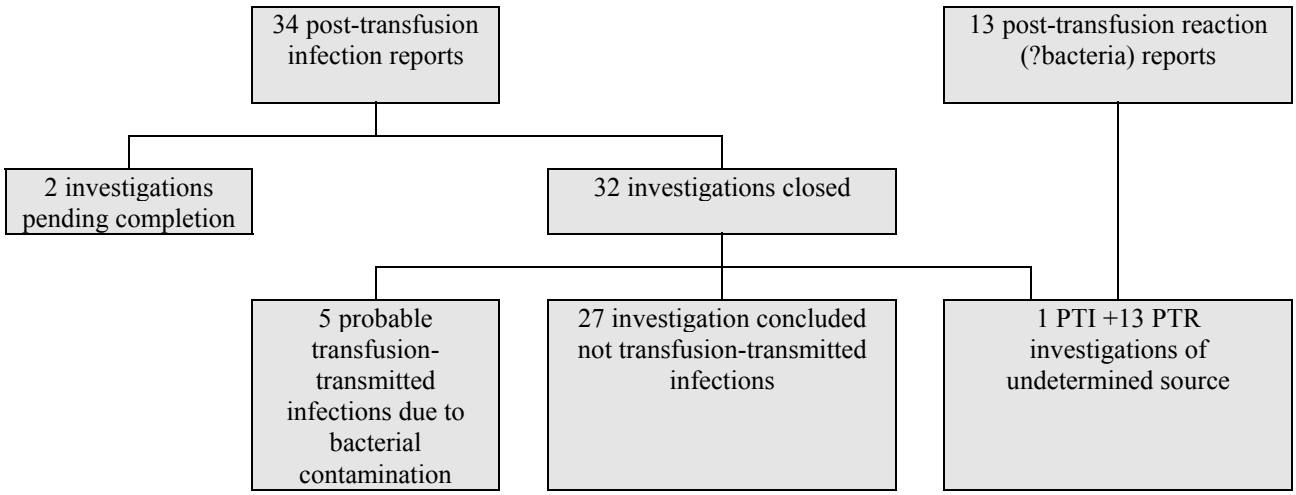
Of the 28 PTI reports received from blood centres in England, Wales and Northern Ireland, 1 HCV infection (4%) was classified as a post-transfusion infection of undetermined source due to inconclusive investigation of the donation(s) implicated as the source of infection. For 20 (71%) PTI reports (10 bacteraemia, 6 HBV infections, 3 HCV infections, 1 HIV infection), investigation was completed and there was no evidence to implicate transfusion as the source of infection. A possible source of infection other than transfusion was known for 5 of these infections: 1 HBV was born and lived in Pakistan; 1 HBV had received a transfusion 36 years ago; 1 HBV had received a transfusion in Shanghai; 1 bacteraemia due to enterocolitis and 1HIV due to maternal transmission. Five (19%) PTI reports were classified as transfusion-transmitted infections due to bacterial contaminations, 4 were transfused in 2001, and one during 2002. Two (7%) PTIs are still under investigation (1 HBV and 1 HCV).

An additional 13 reports were received for post-transfusion reactions that were suspected to be due to bacteria but had no evidence of bacterial infection (or endotoxin) that could have caused the reaction in either the recipient or the implicated component.

Reports from blood centres in England, Wales and Northern Ireland were received from 8 of the total 12 centres; donations made at these 8 centres represent approximately 70% of all donations tested each year in England, Wales and Northern Ireland.

Blood centres in Scotland reported 6 post-transfusion infection investigations during the report year. Two post-transfusion HIV infections and 3 post-transfusion HCV infections were completed and no evidence was found to implicate transfusion as the source of infection. One post-transfusion HCV infection is still under investigation. Scottish cases reported since October 1998 have been included in the numbers of post-transfusion infections and transfusion-transmitted infections shown in the tables and figures here since the 2000/01 SHOT Annual report.

Figure 33
Classification of post-transfusion infections (and post-transfusion reactions) in the UK reported between 1/10/2001 and 31/12/2002.



Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus
No transfusion transmitted HBV infections were reported during this year.

Hepatitis C virus
No transfusion transmitted HCV infections were reported during this year.

HIV
No transfusion transmitted HIV infections were reported during this year.

HTLV
No transfusion transmitted HTLV infections were reported during this year.

B. Infections for which donation testing is not mandatory

Bacterial contamination
Five transfusion-transmitted bacterial contaminations were reported between 1/10/2001 and 31/12/2002. All recipients had major morbidity, none died.

One recipient (61 year old female) developed rigors and restlessness after transfusion with a single 5-day old pooled platelet unit during treatment for myeloma. *Staphylococcus epidermidis* of an identical strain was cultured from the recipient's blood and the platelet pack. Three of the 4 donors who contributed to the unit were swabbed and *S. epidermidis* was cultured from all 3, and the same strain was found on the arm of one donor. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with S. *epidermidis* from the donor's arm.

One recipient (66 year old male) developed fever after transfusion with a single unit of 5-day old pooled platelets. *Staphylococcus epidermidis* was cultured from the recipient's blood and the platelet pack. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with *S. epidermidis:* no source of contamination was identified.

One recipient (28 year old female) developed tachycardia, hypotension and pyrexia immediately after transfusion with a single 5-day old unit of platelets during treatment for thrombocytopenia. *Morganella morganii* was isolated from the recipient and giving set. The probable source of the recipient's reaction was concluded to be a unit of platelets contaminated with *M. morganii:* no source of this contamination was identified.

One recipient (72 year old female) developed an acute wheeze, fever and rigors after the start of transfusion with a 3-day old unit of pooled platelets during treatment for myeloma and acute mylomonocytic leukemia thrombocytopenia. Group B *streptococcus* was isolated from the platelet pack. Culture of throat and arm swabs from the donors of this unit did not isolate any group B streptococcus. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with group B *streptococcus*: no source of this contamination was identified.

One recipient (62 year old male) developed hypertension, fever and rigors during a transfusion with a single 5-day old unit of pooled platelets during treatment for myelodysplasia. *Staphylococcus epidermidis* was cultured from the recipient's blood and the platelet pack but not from the donor's skin. Despite this, the probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with *S. epidermidis* from the venepuncture site of the donor.

Underreporting

The cases ascertained by this surveillance system were diagnosed, suspected to be attributable to transfusion, communicated to the blood service, and reported by a blood centre to the surveillance centre. At any one of these steps, other post-transfusion infections may have been missed and the extent of underreporting of post-transfusion infections is therefore unknown. The proportion of post-transfusion infections that are reported each year may vary as other factors such as testing performed on transfusion recipients, awareness of transfusion as a possible source of infection, reporting of information to blood centres and reporting of information from blood centres to the surveillance centre vary.

Previous years

During the previous reporting year (i.e. 01/10/2000 to 30/09/2001) 4 transfusion-transmitted infections were reported (see SHOT Annual Report 2000-01 for details of these cases).

The investigations of 4 post-transfusion HBV infections that were classified as pending full investigation in the 2000-01 SHOT Annual Report have subsequently been concluded to be not due to transfusion.

Table 43 shows the cumulative number of transfusion-transmitted infections reported by the end of December 2002.

Cumulative data

The cumulative number of PTI and PTR reports received by year of transfusion since October 1995 are shown in Figure 34.

Figure 34
Post-transfusion infection reports by year (Scotland included from 10/98)

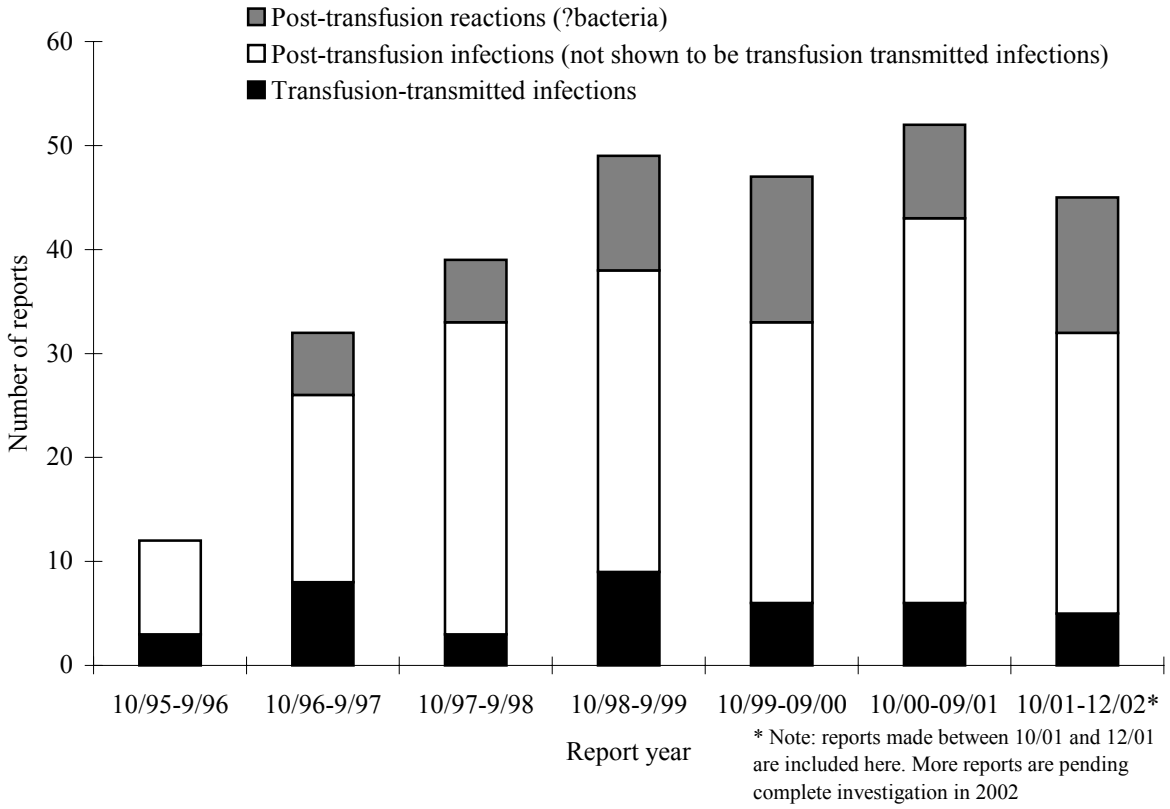


Table 43
Cumulative total transfusion-transmitted infections: reported between 1/10/1995-31/12/2002 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	Pre-1995	1995	1996	1997	1998	1999	2000	2001	2002	Total	Deaths
Infection											
HAV	-	-	1(1)	-	-	-	-	-	-	1(1)	-
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)	2(3)	1(1)	-	-	8(9)	-
HCV	-	-	1(1)	1(1)	-	-	-	-	-	2(2)	-
HIV[c]	-	-	1(3)	-	-	-	-	-	-	1(3)	-
Bacteria	-	1(1)	1(1)	3(3)	4(4)[ax2]	4(4)[a]	7(7)[ax3]	5(5)	1(1)	26(26)	6
Malaria	-	-	-	1(1)[a]	-	-	-	-	-	1(1)	1
HTLV I	1(1)	-	-	-	-	-	-	-	-	1(1)	-
Total[d]	2(2)[b]	2(2)	5(7)	6(6)[a]	5(5)[ax2]	6(6)[a]	8(8)	5(5)	1(1)	40(43)	7

Notes: [a] Infection was implicated in the death of a recipient.
[b] One household member who was caring for the recipient has been diagnosed with acute HBV.
[c] One additional investigation failed to confirm or refute transfusion transmission of HIV infection during the early 1990s. As the patient had received multiple transfusions, and had no other risk factors for infection, transfusion with HIV infectious blood was concluded to be the probable, although unproven, source of infection.

Bacterial contaminations

A summary of the species of bacteria and the type and age of the implicated components for the 26 transfusion-transmitted bacterial contaminations reported between 01/10/1995 and 31/12/2002 are shown in table 44.

Table 44
Transfusion-transmitted bacterial contaminations reported in UK between 01/10/1995 and 31/12/2002 by species and component type and age (N=26).

	Platelets Age (in days) at use							Red cells
	1	2	3	4	5	NK	All	
All species	*0*	*1*	*2*	*6*	*4*	*4*	*22*	*4*
Bacillus cereus				3[a]		1	4	
Coagulase negative Staphylococci					1		1	1 (23 days)
Enterobacter aerogenes			1[a]				1	
Escherichia coli			1[a]			1	2	
group B Streptococcus			1	1		1	3	
Morganella morganii					1		1	
Serratia liquifaciens								1
Staphylococcus aureus					1	1[a]	2	
Staphylococcus epidermidis		1[a]		2	5		8	1 (32 days)
Yersinia entercolitica								1[a] (33 days)

[a] Infection was implicated in the death of a recipient.

Seven of the 22 contaminated platelet units were collected by apheresis from single donors, 14 were recovered from whole blood donations (each from a pooling of four donations) and for one the source of platelets was not known. For 8 of these cases the donor's arm was confirmed by subsequent testing to have been the probable source of the contamination. For some others, investigation of donors' arms was incomplete or inconclusive but the nature of the contaminating organism was suggestive of a skin contaminant that was most likely to have been

introduced to the pack at the time of collection. For 2 cases, the donor's blood was concluded to have been the source of the contamination (i.e. endogenous bacteria, so contamination of the pack not preventable by skin cleansing or diversion).

Cumulative data about Hepatitis B virus transmissions

Since October 1995, 7 of the 8 transfusion-transmitted HBV infections reported have been concluded to be probably due to infectious blood collected from donors with acute HBV infection, with only one (reported in the first reporting year) due to infectious blood from a donor with later stage HBV infection. This is a change from that observed in earlier collations of transfusion-transmitted HBV infection. For example between 1991 and 1997 only 3 of 14 transfusion-transmitted HBV infections reported to the Health Protection Agency were found to be due to donations from donors with acute infection, with the majority being due to donations from donors with chronic infection[18]. This change has implications for the choice of strategies to further reduce the risk of transfusion-transmitted HBV infection.

COMMENTARY

- Due to the adjustment in reporting year, reports made over a 15-month period from October 2001 to December 2002 are included in this report. Despite this extended period, the numbers of post transfusion infections reported were fewer than reported in the previous report year (43 reported between October 2000 and September 2001). Reasons for this may include variation in testing, diagnosing and reporting practices for infections in transfusion recipients. The number of these that are later classified as transfusion transmitted infections, however, is unchanged and suggests consistent sensitivity in the surveillance of these.

- Reported transfusion-transmitted infections are rare: only 5 confirmed cases were recognised in the UK during this 15-month period of reporting. Investigations of a further 28 cases of post-transfusion infection were reported. The majority (86%) of the closed PTI investigations reported during this period were not caused by transfusion.

- 13 cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported (in England, Wales and Northern Ireland). Conclusive investigation of a suspected bacteraemia in a transfusion recipient relies heavily on the collection and handling of relevant samples at the hospital where the transfusion was performed. This means that absence of evidence of an infection (or toxin), in donations given to recipients who had post-transfusion reactions that were suspected (on clinical presentation) to be due to bacteria does not equate with evidence of absence of a transfusion-transmitted infection (or toxin).

- Cases of transfusion transmitted bacterial infections have continued to be reported subsequent to the introduction of universal leucodepletion.

- Most bacterial contaminations are due to skin flora entering the pack at the time of collecting the donation

- In August 2002, the NBS began screening all blood donors for HTLV. Transfusion-transmitted HTLV infection has been previously documented in UK[19]. Leucodepletion may have reduced the risk of HTLV transmission by transfusion since these cases were transfused[20]. A 'lookback' at the serological status of any infected donors and the fate of these units is to be carried out and will be reported elsewhere.

- Numbers of reported cases are small and fluctuations in reports are to be expected. Also, the reporting system is probably biased towards infections that cause rapid onset of acute disease. However, it should be noted that bacteria have accounted for the majority of reported transmissions by transfusion and the majority of known deaths due to transfusion transmitted infections in the cumulative data.

- The absence of any reports of transfusion transmitted HCV (or HIV) infections is consistent with the expected low risk of an HCV infectious donation entering the blood supply in the presence of the current testing of blood donations for both anti-HCV and HCV RNA (and anti-HIV).

RECOMMENDATIONS

- **Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components. These include implementation of diversion of the first few mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site) and improvements in cleansing of donors' arms. Methods for testing platelets for bacterial contamination should be evaluated. The risk of transfusion of a contaminated component can be reduced by adherence to BCSH guidelines (1999)[6] with regard to the visual inspection of units for any irregular appearance immediately prior to transfusion (particularly platelets);**

- **Hospitals should consult guidelines and the blood service about the investigation of transfusion reactions suspected to be due to bacteria. National guidelines on the investigation of these cases are available from all NBS centres. Cases that are inconclusive due to discard of the implicated pack before sampling continue to be reported, therefore particular attention should be paid to the sampling and storage of implicated units.**

- **The Standing Advisory Committee for Transfusion Transmitted Infections (SACTTI) is currently reviewing the residual risk of transfusion transmitted HBV infection to assess the need for additional screening methods, such as HBV RNA testing and/or anti-HBC.**

18. SERIOUS HAZARDS OF TRANSFUSION EVENTS REPORTED IN PATIENTS LESS THAN 18 YEARS OF AGE.

DEFINITION

A validated case reported to SHOT involving a patient less than 18 years of age.

A total of 1630 analysable reports have been received by SHOT from its introduction in October 1996 to the end of December 2002 (6 years and 3 months) Of these 141 (8.65%) involved patients less than 18 years of age. Epidemiological studies of transfusion recipients[21] suggest that the frequency of adverse events may be disproportionately high in this age group.

In paediatric practice the transfusion of blood and blood components is concentrated to a small number of high user specialities, primarily neonatal medicine, extracorporeal membrane oxygenation, haemato-oncology, intensive care and cardiac surgery. Outwith these specialities the transfusion of blood and blood components is uncommon and this may lead to less awareness of transfusion related hazards. There are a number of areas where transfusion practices vary between adults and children, particularly when infants are the recipients ie blood component selection and specification. It is of interest to determine if this increases the potential for error. Analyses of reported cases for patients less than 18 years of age show the distribution of cases to be similar to that seen over all age groups (table 45) with the exception of Delayed Transfusion Reactions and Post Transfusion Purpura.

Table 45 shows the categories of adverse events reported and the relative proportions over the first 6 years 3 months of SHOT reporting.

Table 45

Nature of Adverse Events Reported	Proportion of all reports in the first 6 years	
	All ages	Less than 18 years
Incorrect Blood Component Transfused (IBCT)	63.9%	80.1%
Acute Transfusion Reactions (ATR)	12.2%	10.6%
Delayed Transfusion Reactions (DTR)	11.5%	0.7%
Transfusion-Related Acute Lung Injury (TRALI)	6.6%	6.4%
Transfusion-Associated Graft-Versus-Host Disease (TA-GVHD)	0.8%	1.4%
Post-Transfusion Purpura	2.5%	0%
Transfusion-Transmitted Infection (TTI)	2.2%	0.7%

AGE

Age was highly relevant. 61/141 or 43% of cases occurred in infants less than 1 year of age, with 35/53 or 66% involving infants in their 1st month of life. Neonates are a highly transfused patient population, and these findings reflect this. The incidence of the two commonest reported events, IBCT and ATR, was similar across the paediatric age group. There was only one case of DTR reported and this was in a child over the age of 10 years. TRALI was not reported in the first year of life and post transfusion purpura was not reported at all in patients less than 18 years of age (table 46).

Table 46

	No of Cases	Incident Type					
Age		**IBCT**	**ATR**	**DTR**	**TRALI**	**TA-GVHD**	**TTI**
<1 day	14	14					
1 day-1 week	13	11	2				
1 week – 1 month	14	10	3			1	
1 month – 1 year	20	18	2				
1 -5 years	22	18	1		3		
5 -10 years	16	13	1		2		
>10 year	41	29	6	1	4	1	
"child" NOS	1						1
Total	**141**	**113**	**15**	**1**	**9**	**2**	**1**

NOS = Not otherwise specified

OUTCOME

There were 5 deaths due to transfusion related events amongst the 141 reported cases

- 3 due to TRALI
- 2 due to TA-GVHD

There were a further 6 deaths from unrelated causes amongst the 141 reported cases.

In addition, 13 patients suffered significant morbidity or have a risk of future problems due to RhD sensitisation.

INCORRECT BLOOD COMPONENT TRANSFUSED (N=113)

Age, sex and outcome data are given for 113 patients in the age range <1 day to 17 years. Seventy-four reported cases involved children less than 6 years of age and more detailed analysis is presented for these children. One 17-year old female was being treated for a post-natal haemorrhage and would not have been managed in a paediatric ward.

Sex of patient-

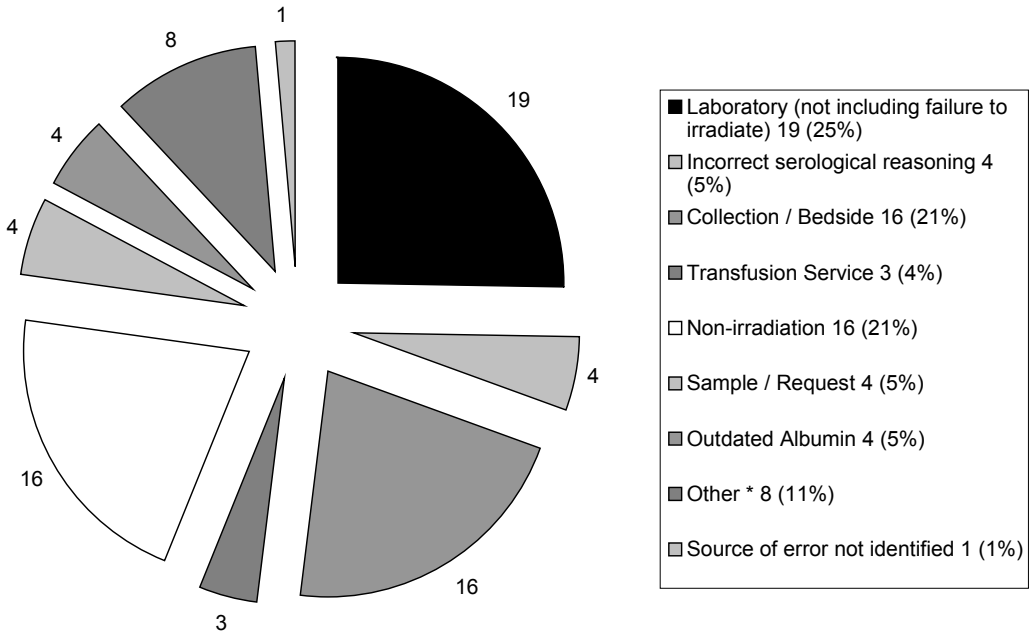
58 female
55 male.

Outcome in IBCT group

- 91 patients suffered no sequelae as a result of receiving an incorrect blood product
- 14 patients suffered morbidity or potential morbidity but recovered and this group included 2 patients who developed intra-vascular haemolysis
- 6 patients died of their underlying condition
- 2 reports stated no outcome

Analysis of the children under 6 years of age (74 cases)

Figure 35
Errors reported (n = 75)



*3 x right product transfused despite incorrect details on unit or request
1 x red cells used were too old for an exchange transfusion
1 x misinterpreted prescription for RBCs 50 mL to be given over 4 hours as 50 mL per hour for 4 hours
1 x 8 paedipacks transfused instead of 1 adult unit
1 x false low Hb from a diluted sample – transfusion unnecessarily
1 x bag punctured by inadequately trained staff carrying out an 'audit'

The distribution of incidents within the IBCT group show some differences across the age groups. Laboratory errors (25=19 laboratory errors +6 incidents of failure to irradiate by laboratory) and failure to request irradiated components (10) accounted for 47% of the total errors in those under 6 years of age. Errors of sampling, requesting, collecting and administrating appear less frequent than in the adult population.

Examples of IBCT errors include-

1. Three group A or B recipients were given group O FFP (laboratory error in 2 cases, anaesthetist error in 1 case). The assumption that Group O plasma is appropriate for all recipients is a recurring error in SHOT reports.

2. Three patients received untreated FFP who should have received pathogen inactivated FFP; SDFFP (1 case) and methylene blue FFP (2 cases).

3. Three babies who had had previous intrauterine transfusions were given non-irradiated blood. The laboratory and medical staff were unaware that infants who had had an intrauterine transfusion should thereafter receive irradiated cellular blood products.

4. Excessively old blood was issued for exchange transfusion (1 case) and not red cells of 5 days or less of age.

Ten patients under 6 years of age suffered significant morbidity. These included 4 RhD negative girls who have been exposed to RhD positive red cells and who may therefore be sensitised and have problems in future pregnancies (Table 47).

Table 47

Case no.	Product	Group of product	Group of patient	Error	Outcome
1.	RBC	O RhD pos	O RhD neg	Laboratory group error	Possible sensitisation
2.	RBC + platelets	O RhD pos	A RhD neg	Laboratory group error	Possible sensitisation
3.	RBC	A RhD pos	O RhD pos	Laboratory group error	Haemoglobinuria
4.	RBC	A RhD pos	B RhD neg	Laboratory group error	Fever, rigors, loin pain
5.	RBC	O RhD pos	O RhD neg	Selection error	Possible sensitisation
6.	RBC	---	---	Cells too old for exchange transfusion	Cardiac problems and electrolyte imbalance
7.	platelets	O	B	Transfusion Service sent grp O platelets for a group B patient without checking for high titre. The unit was very high titre.	Acute reaction, fever, rigors. Hb fell from 9.8 to 4.0
8.	RBC	O RhD pos	O RhD neg	Laboratory issue error	Possible sensitisation
9.	FFP	O RhD pos	O RhD neg	Laboratory selection error	Possible sensitisation
10.	RBC	---	---	Failure to request irradiated products	aborted stem cell harvest. Pt had apheresis line inserted before the procedure was abandoned

IMMUNOLOGICAL COMPLICATIONS

Acute Transfusion Reactions (N=15)

Age range: 2 days – 17 years (4 patients <1 month)

Components transfused: platelet concentrates in 3 cases, FFP in one case and red cells in 11 cases.

Aetiology of reaction – In a number of cases no clear cause of the reaction was identified.

Case 1 **(see also chapter 12 case 9)**

A 2.2kg male infant underwent a switch operation at 4 weeks of age for transposition of the great vessels. Pre-operative and post-operative WCCs were normal. On the 2nd post-operative day he received 80mls of red cells in OAS containing approximately 12.5ml/kg of plasma. Two hours after completion of the transfusion his WCC had fallen to $0.7x10^9$/l with a neutrophil count of $0.06x10^9$/l. The neutropenia was confirm by repeat count and persisted. A bone marrow aspirate 48 hours after transfusion showed active myelopoiesis to the stage of metamyelocytes with no band or segmented forms. He received Granulocyte colony-stimulating factor (G-CSF) and remained clinically well with no fever or signs of infection. In addition he had no respiratory distress, a normal CXR and no typical signs of TRALI. The donor plasma was found to contain antibody to Human Neutrophil Antigen 1b (HNA 1b) with no other white cell antibodies. The patients neutrophils were HNA 1b positive by DNA typing. The donor was an untransfused multiparous female whose genotype was HNA 1a/1a and her husband's genotype HNA 1b/1b. This case adds strength to the argument for excluding multiparous female donors.

Case 2 **(see also chapter 12)**

A 5-month old infant with pneumonia was transfused 15ml/kg red cells in optimum additive solution (OAS). Within 2hours of completion of the transfusion the infant became tachypnoeic and acidotic. The infant's post-transfusion DAT was negative as was the antibody screen. It was unclear if the acidosis was related to the transfusion but the anticoagulant/suspension solution may have been contributory.

Case 3 **(see also chapter 12 case 3)**

A 10-year old girl developed autoimmune haemolytic anaemia (AIHA) two months after a cord bone marrow transplant. She was transfused 2 units leucocyte depleted red cells. During the transfusion she developed back pain and passed dark urine. The transfusion was stopped and she received a diuretic. Her haemoglobin fell, she became jaundiced, had haemoglobinuria and her renal function deteriorated. Her DAT was positive pre-transfusion with IgG and complement coating her red cells. The findings were similar when a post transfusion sample was tested. The transfusion was thought to have exacerbated post transplant AIHA.

Other causes include:

- Immune reaction to a plasma protein
- IgA deficiency with anti-IgA
- Excessive infusion rate (increased by patient in order to attend social function)

All patients recovered with no residual effects.

Delayed Transfusion Reaction (N=1)

Case 4

A 17-year old girl with infection and a sickle cell vaso-occlusive crisis was transfused 2 units of RBC concentrates. She had been transfused on three previous occasions and most recently more than a year earlier. Post-transfusion she developed a fever, became jaundiced and her haemoglobin fell. She was transferred to ICU where she was observed for 24 hours. Her antibody screen, which pre-transfusion had been negative, was positive with IgG coating the red cells. The specificity of the antibody could not be identified in the post-transfusion sample. She survived with no sequelae. As a result of this incident, it was agreed that all sickle cell patients should have RBC genotyping performed during their steady state.

Transfusion-Related Acute Lung Injury (N=9)

There may be considerable diagnostic difficulty , particularly in infants, due to similar clinical findings in a number of conditions causing acute respiratory compromise.

Age range : 2 – 17 years

Components transfused : FFP in 3 cases, platelets concentrates in 3 cases , platelet concentrates and FFP in 1 case, not stated in 2 cases

Mortality : 3 patients died – possibly attributable to TRALI
1 patient recovered but with impaired respiratory function
5 patients made a full recovery

Graft-versus-Host Disease (N=2)

2 cases of GVHD were reported.

Case 5

A 13-day-old baby, born at 32 weeks received non-irradiated red cells from a donor who was later found to have HLA-haplotype sharing with the infant. The infant died 2 weeks later. There was some evidence to suggest that the infant had a form of severe combined immunodeficiency.

Case 6

A 14-year old girl with relapsed acute lymphoblastic leukaemia received 2 units of non-irradiated red cells and 2 units of non-irradiated platelets, followed by irradiated components. She later died of GVHD.

Both patients with TA-GVHD died, as have all patients with TA-GVHD reported to SHOT.

Transfusion Transmitted Infection (TTI)

Only one case of transfusion –transmitted infection has been reported within the paediatric age group in the 6-year span of SHOT. This child (age not given) experienced a bacteraemic reaction to a 5-day-old unit of platelets (*staph.epidermidis*) but recovered without sequelae. No virus transmissions in children have been reported.

COMMENTARY

- Adverse reactions to transfusion in childhood are not particularly uncommon; 8.65% of all cases reported to SHOT.

- 61/141 (43%) of cases occurred in infants less than 1 year of age, with 35/53 (66%) involving infants in their first month of life. This reflects the pattern of transfusion in the paediatric population, in particular the relative high incidence of transfusion in the neonate because of the complications of prematurity and congenital malformations.

- Infants in their first year of life may require special consideration of component selection or component manipulation, including the avoidance of red cells in additive solutions for exchange or large volume transfusion, selection of CMV-negative units, irradiation of cellular components following IUT, selection of pathogen inactivated FFP, matching against maternal antibodies etc. It is clear from some of the reported errors that there is lack of awareness amongst laboratory, nursing and medical staff of the special needs of infant recipients of blood and blood components[11, 12]. Of the 14 errors that were felt to be due to lack of awareness of special requirements, 8 arose in the laboratory.

- Errors arise due to failure to identify patients at the time of sampling and administration. Wristband checks are of paramount importance in younger children who are unable to identify themselves verbally.

- A wide range of immunological reactions were reported in children, including 7 acute transfusion reactions in neonates. Children may have difficulty communicating transfusion-induced distress, other than in a non-specific manner. Neonatal adverse reactions may be non-specific in their presentation (e.g. hypoxia and acidosis as a non-specific reaction to a range of disorders) so a high index of suspicion is needed. Delayed haemolytic transfusion reactions are not common in childhood, in part because those transfused in the neonatal period rarely make antibodies and older children may be transfused on only one occasion. Similarly, post-transfusion purpura, which arises in those already sensitised to platelet antigens by pregnancy or, rarely, by transfusion, was not reported and appears to be primarily a problem of adults.

RECOMMENDATIONS.

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

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

- **Children receiving blood components should be closely monitored, as in adult practice, with appropriate baseline recordings and an early check 15 minutes after commencing each new unit.**

- **BCSH transfusion guidelines are as applicable to children as adults and should be followed.**

- **Paediatricians should be encouraged to report suspected transfusion-related adverse events in their patients to the SHOT scheme and to disseminate lessons learned from this to their staff.**

19. ACKNOWLEDGEMENTS

Once again we are indebted to several individuals and organisations for their continuing help and support. The Steering Group would like to take this opportunity to thank them for their contributions without which the publication of this sixth annual SHOT report would not have been possible.

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The SHOT office staff:

Aysha Haque, Data Collection and Management Officer
Rebecca Hornby, Personal Assistant to Hilary Jones until November, 2002
Helen Phillips, Personal Assistant to Hilary Jones from May, 2003

Blackwell Publishing for permission to reproduce figure 18 in chapter 9

Professor Adrian Newland, Barts and The London NHS Trust for permission to reproduce the paper in appendix 9

Dr. C R M Hay, UKHCDO for providing the paper in appendix 10

Dr. N Smith, Chair, NBS Transfusion Medicine Clinical Policies Group for the guideline reproduced in appendix 11

All those hospitals who have participated in SHOT reporting

Without your support, SHOT would not be possible

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RESOURCES REQUIRED FOR THE IMPLEMENTATION OF BETTER BLOOD TRANSFUSION HSC 2002/009

The resources required to implement Better Blood Transfusion 2 will be quite variable depending on the size of the hospital and the level of transfusion dependent activity undertaken. It is expected that many organisations will have already managed to achieve some of the objectives outlined and that fewer additional resources will be required. However, a complete programme is described to achieve the ideal, to give an overview of the potential complexity of the process. The importance of this is that it is clear that any examination of transfusion related procedures commonly raises issues that have not been previously contemplated, therefore this paper covers all areas that should be considered. In particular, medical and nursing knowledge is frequently overestimated and this can impact on all aspects of transfusion practice.

The resources can be categorised into five headings. It is unrealistic to assume that all items will be in place by April 2003 but the list, by describing the ideal, will permit a hierarchy of goals to be planned, which can be worked toward. Aside from the equipment, all expenses will be recurring. *Appendix 1* tables a proposed hierarchy of need with attendant costs.

STAFF

Transfusion Practitioner

This role is vital for the organisation and provision of staff training, implementation of safe practice and assessment of appropriate usage. The postholder may be from a medical, biomedical scientist or nursing background and there are pros and cons attached to each. Depending on the size of the hospital there may need to be one or several people in post and in the larger Trusts the post should work in tandem with an Audit Coordinator (see below) . In this instance, consideration should be given to the advantages of individuals from complementary disciplines e.g. nurse and biomedical scientist or audit co-ordinator and nurse. Pertaining to nurses, each Trust has it’s own

criteria for grading relating to remit and scope of practice. Post holders range from G – I.

All members of the HTT will require funding for study leave in order to develop and maintain the necessary skills and knowledge base to be effective in post.

Audit Co-ordinator

Audit plays a pivotal role in establishing an evidence base regarding local transfusion practice. As a minimum this should encompass review of the maximum surgical blood order schedule and compliance with policies and protocols. More specific projects could explore alternatives to red cell transfusion and the healthcare economics of changing and modifying practice.

In smaller hospitals the audit component may be undertaken as part of the biomedical scientist's or transfusion practitioner's duties. In larger hospitals serious consideration should be given to the advantages of a dedicated audit co-ordinator.

Lead Consultant for Transfusion

It is probable that all hospitals have a designated consultant responsible for blood transfusion. However, it is possible that there are no dedicated sessions. Between one and four sessions per week will be required depending on the volume of transfusion related activity undertaken.

As a guide the distinction in hospital size used by the Joint Intercollegiate Committee on Haematology and the British Society for Haematology in producing the document on 'Haematology Consultant Manpower in the 21st Century' should be used to determine sessional commitment. The smaller DGHs will require only one dedicated session, whereas the larger DGHs and the teaching hospitals will need at least four. In the latter, where the clinical activity is unusual or there is a particular interest, one WTE could be justified.

Biomedical Scientists

There needs to be adequate numbers of biomedical scientists trained in blood transfusion if these are not currently part of the establishment. This should enable good laboratory practice and participation in national accreditation schemes, and ensure the blood bank manager has time to fulfil their role in the Hospital Transfusion Team (HTT).

I.T. SUPPORT

The laboratory computer system must provide adequate and robust functionality in order to enable data retrieval for both audit purposes and participation in the Blood Stocks Management Scheme. This issue becomes more significant in the context of integrated pathology systems.

There must be adequate I.T. support for all members of the HTT. Audit software may be beneficial in the development and analysis of questionnaires in particular. A laptop computer would be an advantageous tool in the collection of raw data for audit purposes. Combined with a data projector it would become invaluable in the delivery of educational programmes. A considerable amount of time can be saved by updating lectures in a PowerPoint format as opposed to OHP acetates. It also allows for the screening of information in a DVD format negating the need for transporting unwieldy television and video equipment to teaching sessions.

The costs identified in Appendix 1 may appear excessive as cheaper options are available in retail outlets. However, computer equipment that is not purchased via a hospital I.T. department may not be covered by their support and maintenance services.

CLINICAL EQUIPMENT

Computerised blood fridge monitoring is expensive, but the Trusts that have introduced this technology believe it makes a noteworthy contribution to blood stocks management. The level of 'out of temperature control' red cells is often underestimated. It is not unusual, on the appointment of a transfusion practitioner, for this figure to increase with improved staff awareness.

Computerised bedside monitoring technology can be applied to both the sample labelling and the administration aspects of transfusion practice. Indeed, the technology can also be applied to other aspects of clinical care including drug administration, which may make it a more attractive proposition. It may not be necessary to introduce this to all clinical areas however, some areas will need more than one device.

STATIONERY

Patient information

Patient information leaflets are provided by the National Blood Service, but an increasing number of hospitals will require translation of patient information. At Barts and The London where the local population speak 140 languages it is impractical to provide translation into all dialects. The Trust's Patient Advice and Liaison Service recommend that a statement be added to English leaflets advising who to contact. As it costs £500 for a two line translation this is generally limited to the six most prevalent languages. The use of audio cassettes should be explored but the logistics of ensuring that tapes and playback facilities are available in all areas are complex. It may be more effective to provide an adequate language interpreting service.

Minimum data set labels

Audit has demonstrated that documentation of transfusion episodes in the medical notes is inadequate. A pre-printed adhesive label with prompts detailing the minimum data set required may improve compliance.

Teaching consumables

Funding needs to be secured to support all educational activities including posters, handouts, videos etc.

ALTERNATIVES TO TRANSFUSION

In addition to the costs outlined above additional resources will be required to fund alternatives to transfusion. In the context of this document it is not possible to attribute costs. The hierarchy of need will be determined by local clinical activity.

Cell salvage

Development of a cell salvage programme is likely to be limited by the number and skill mix of staff available in theatres, ITU and A&E, and the cost of the machines and consumables. Companies supplying the equipment now market these machines for under £5000 or provide lease purchase options where the cost of the machine is spread over the cost of disposables. There are a few private companies that offer cell salvage services for hospitals who could not justify the expense of setting up an in house programme. Obviously this will be limited by geographical location.

Post operative drainage/re-infusion devices

Several studies have shown that these devices are effective, particularly around orthopaedic surgery. The cost is per unit is approximately £48.

Pharmacological agents

Whilst there is clearly a role for erythropoietin and anti-fibrinolytics in particular it is difficult to make accurate predictions regarding the use of these agents.

Professor Adrian Newland
Dr Drew Provan
Emily Okukenu (Transfusion Nurse Specialist)

Barts and The London NHS Trust
September 2002

APPENDIX 1 Hierarchy of need with attendant costs

	ITEM	COST (£)
ESSENTIAL	Dedicated biomedical scientist	BMS1 20,200 BMS2 25,600 BMS3 31,300
	Transfusion Practitioner (nurse)	G 29,500 H 32,300 I 35,900
	Lead Consultant (per session)	6,000
	Desktop computer and printer	1,128
	Study leave expenses for HTT	5,000
HIGHLY DESIRABLE	Teaching consumables	3,000
	Audit co-ordinator (A&C 6)	25,000
	Laptop computer	1,950
	Data projector	3,082
	Minimum data set labels (40,000)	370
	Audit software	935
	Translated patient information	5,000
DESIRABLE	Computerised blood fridge monitoring for 5 fridges (including system manager software)	46,140
	Computerised bedside monitoring – labelling samples/administration (for 50 units)	73,437

Pay does include on costs (employer's N.I. and superannuation @7%). It does not include Cost of Living Supplement or London Weighting. All posts are quoted at mid point to the nearest £100.

Costs per unit are based on quotes provided for Barts and The London NHS Trust.

UKHCDO

Adverse events related to treatment of haemophilia and related disorders

October 2001 – December 2002 inclusive

Address for correspondence: Dr CRM Hay, Consultant Haematologist and Chairman, UKHCDO Data Management Group, Haemophilia Comprehensive Care Centre, Cobbett House, Manchester Royal Infirmary, Oxford Road, Manchester, M13 9WL.

Report on recent adverse events:

- *2 Hepatitis C transmissions*

  These were new reports but not new infections. They represent the discovery of hepatitis C, contracted many years before, in patients subsequently lost to follow-up.

- *9 new inhibitor antibodies to factor VIII in patients with congenital heamophilia*

- *1 report of a thrombotic event / DIC*

  Currently under investigation – No details available

- *1 report of a transfusion reaction*

  This was a moderate reaction with feeling cold and shaking, following the administration of Benefix (recombinant FIX).

There were no other reports of adverse events of blood products or clotting factor concentrates.

TRANSFUSION RELATED ACUTE LUNG INJURY (TRALI)

Prepared by: S.MacLennan for the NBS Transfusion Medicine Clinical Policies Group.

Membership: N Smith (Chair), A Copplestone, M Gesinde, S MacLennan, C Morgan, A J Mortimer, M F Murphy, W Ouwehand, D H Pamphilon, M de Silva, D Stainsby, R Warwick, L Williamson

Version 8 Date: 18/03/2003

Approved by National Blood Service Transfusion Medicine Clinical Policies Group on 5th March 2003. To be reviewed no later than March 2005

Purpose

To define the procedure within the NBS for investigation and further transfusion of suspected cases of Transfusion Related Acute Lung Injury, and subsequent management of implicated donors.

Method

Recommendations are based on review of the literature and review of accepted current clinical practice. The definitions of the types of evidence and the grading of recommendations used in this document originate from the US Agency for Health Care Policy and Research and are provided in the Appendix.

Consultation

NBS Transfusion Medicine Clinical Policies Group

NBS Transfusion Medicine Clinical Policies H&I / PGI (TRALI) Subgroup (Membership: Geoff Lucas, Sheila MacLennan, Edwin Massey, Cristina Navarrete, Willem Ouwehand, Nay Win)

NBS Components Strategy Group

Status

Approved by the Transfusion Medicine Clinical Policies Group on 5th March 2003

Summary

TRALI is a serious complication of blood transfusion which is thought to arise as a result of the interaction of specific leucocyte antibodies with leucocytes in most cases (Evidence Level Ib). Susceptibility of some patients may be increased by contributory factors such as underlying disease or modes of treatment, though these factors are as yet poorly defined (Evidence Level IV). Patients present with dyspnoea, hypoxia,and symptoms and signs of pulmonary oedema. Diagnosis is made on clinical grounds, which may later be supported by demonstrating the presence of leucocyte antibodies, most commonly in the serum of donors but also occasionally in the patient. Treatment requires stopping the transfusion and giving oxygen and cardiovascular support. Most cases require mechanical ventilation for several days.

Investigation of each case should be undertaken by designated NBS staff so that each case is uniformly and appropriately investigated. Samples from the patient and donors (restricted initially to female and transfused male donors) of components transfused in the 6 hours preceding the onset of TRALI are investigated for the presence of leucocyte antibodies. The relevance of a positive antibody result is confirmed by either demonstrating that the patient is positive for the corresponding antigen, or that a crossmatch between donor and patient is positive.

A donor who is thought likely to have been implicated in a case of TRALI is resigned from the donor panel (Grade of Recommendation C, Evidence Level IV).

1. Introduction

TRALI is a life threatening complication of transfusion indistinguishable from the Acute Respiratory Distress Syndrome (ARDS) or its less severe form, Acute Lung Injury (ALI) (1). Although rare, TRALI is a significant cause of transfusion associated morbidity and mortality and has been reported as the third most common cause of a fatal transfusion reaction (2). The incidence of TRALI has been reported as 0.02% of all units, or 0.16% of all patients transfused though it may be under diagnosed (1).

2. Pathogenesis

TRALI is thought to result from the interaction of specific leucocyte antibodies with leucocytes. Human Leucocyte Antigen (HLA) antibodies, both Class I and Class II, and antibodies to Human Neutrophil Antigens (HNA) have all been implicated. (3). Multiparous women have been shown to have a higher rate of HLA sensitisation with increasing number of pregnancies (4) and plasma from multiparous women has been demonstrated to play a part in causing impairment of pulmonary function in a randomised controlled trial (5) (Evidence Level Ib). The antibodies are usually donor-derived, though there have been occasional reports of the syndrome occurring after transfusion of donor leucocytes which have interacted with either patient-derived antibodies or antibodies transfused in a second donation, or the presence of HLA antigen/antibody incompatibility in a pooled platelet concentrate. Not all transfusions from donors found to have leucocyte antibodies result in TRALI – even if there is a match of antigen and antibody specificity overt lung injury does not always ensue. It is likely, although not proven, that patient factors may contribute to the development of the syndrome - the requirement of a second “hit” has been postulated in addition to the presence of leucocyte antibodies (6). Hypoxia, recent surgery, cytokine therapy, active infection or inflammation, massive transfusion, and biologically active lipids present in stored, but not fresh, cellular components have all been implicated. The transfusion of leucocyte antibodies itself may act as a second “hit” in a patient whose leucocytes are already primed by other risk factors such as cardiopulmonary bypass or sepsis.

TRALI is clinically indistinguishable from ARDS, which is a type of rapidly progressive and severe respiratory failure that may follow a number of direct and indirect insults to the lung. Post-mortem studies show the pathophysiology of ARDS as being one of diffuse damage to alveolar units (7). Both epithelial and endothelial injury occurs and the alveolar spaces are filled with fluid and proteinaceous debris. Histology shows an intense acute inflammatory cell infiltrate composed of neutrophils and monocytes migrating across the pulmonary vascular bed into the alveolar spaces. The disease is thought to result from initial activation and damage to the pulmonary endothelial/epithelial interface by systemic inflammatory stimuli (both the cellular and circulating mediators) which then stimulate production of further pro-inflammatory mediators and further recruitment of inflammatory cells. ARDS is therefore, the final common presentation following a range of non-pulmonary insults. The question why the lungs are the end organ of choice in TRALI has remained unanswered. A simple rheological explanation may be that where an activating antibody is infused the first microcirculatory encounter is with the narrow diameter capillaries in the lungs. Secondly, the binding of antibodies to mononuclear and polymorphonuclear cells may cause activation partially via the binding of the Fc domain of the antibody to the Fcγ receptor and possibly via the activation of complement. Activated granulocytes and monocytes become stickier as adhesion molecules change from their non-active to their active configuration.

3. Clinical presentation and management

TRALI is characterised by symptoms and signs of dyspnoea, cyanosis, hypotension, fever, (none of these is universal) and pulmonary oedema. The whole blood count may reveal a leucocytosis although this may be preceded by leucopenia. The onset of symptoms occurs usually within 6 hours, but may be up to 24 hours, of a transfusion episode. All blood products including red cells, platelets, plasma, cryoprecipitate and IvIg have been reported to cause TRALI.

The problem for clinical diagnosis is that there are no definitive tests and often transfusion has been performed in clinical settings where other causes of Acute Lung Injury are present (e.g. trauma, sepsis). The differential diagnosis is from acute pulmonary oedema due to fluid overload/left ventricular failure, or ARDS secondary to other causes. The distinction between TRALI and cardiac failure will be aided by measurement of the left atrial pressure (PAWP) which is typically normal or low in TRALI. A low PaO2/FiO_2 Index (<300 mmHg – acute lung injury, <200 acute respiratory distress syndrome) is helpful. The development of pulmonary infiltrates on chest X-rays are not specific. The diagnosis is essentially a clinical one and should be suspected if other reasons to explain the severity of pulmonary oedema are not present. Later, investigations for leucocyte antibodies may support the diagnosis.

There is no specific treatment for TRALI. If the transfusion is still continuing, it should be stopped and oxygen and supportive therapy started. As with ARDS/ALI from other causes the precipitating cause should be removed as soon as recognised. Thereafter treatment is largely supportive to allow time for lung injury to subside. Most cases require mechanical ventilation for several days. Appropriate cardiovascular support should be given. Steroids have been advocated but proof of efficacy is lacking.

4. Data from Serious Hazards of Transfusion haemovigilance scheme (SHOT)

Over the first five years of SHOT 70 evaluable cases were reported. Some were later considered after review not to be TRALI, illustrating the difficulty of making a positive clinical diagnosis of the condition. In 18 cases, TRALI was thought either likely or possibly to have contributed to the patient's death. Haematological malignancy was the most common underlying diagnosis (26 patients) followed by elective surgery (including cardiac surgery) (24 patients). However, it is as yet unclear whether these diagnoses are truly over-represented in TRALI cases, or whether they simply reflect groups of patients heavily exposed to FFP/platelets. Red cell components were implicated in 19 cases, platelets alone in 12, FFP in 19 and combinations of components were transfused in the remaining cases where an implicated component was identified.

5. Components implicated in the development of TRALI

TRALI has been reported to occur after transfusion of all the following blood components; plasma, platelets, whole blood, cryoprecipitate, concentrated red cells and blood in additive solution (Evidence Level III). Proportionate to the numbers of different components transfused, components containing more plasma such as platelets and FFP are more likely to cause TRALI, but the syndrome may also occur after transfusion of components containing smaller volumes of plasma, e.g. SAG-M red cells.
One case of TRALI following infusion of IvIg has recently been reported (Evidence Level III) (8). TRALI has not been reported following the transfusion of pooled plasma products, e.g. solvent-detergent treated FFP. Theoretically, the pooling process may be considered to reduce the risk due to dilution of donor leucocyte antibodies.

6. Referral of Cases

TRALI should be suspected and investigation considered for patients fulfilling the following criteria:

1. Hypoxia
2. Pulmonary infiltrates on CXR
3. Lacking clinical evidence of fluid overload or other cause of pulmonary shadowing
4. Occurrence within 6 hours of blood component transfusion

Any suspected case should be referred initially to one of the medical staff in the local Blood Centre by the hospital blood transfusion department or clinician, who will refer the case to a designated H&I / PGI consultant. Full clinical details will be requested in order to assess the likelihood of the reaction having been due to TRALI. Details obtained should include the following

- patient demographic details
- consultant / hospital
- nature of transfusion reaction and time in relation to transfusion
- components transfused (including donation numbers) in the 24 hours preceding the reaction
- treatment given including ventilation
- clinical response / outcome

Referring consultants should be encouraged to report the incident to SHOT IF TRALI remains the most likely diagnosis and they should be reminded of this in the final report following laboratory investigations.

On receipt of the referral, the designated NBS consultant will:

- open an investigation file
- inform the local H&I and the national Granulocyte Immunology laboratory by e-mail about the case
- request samples from the patient
- review clinical details, obtaining more from other sources if necessary (e.g. ITU staff) to assess likelihood of the reaction being TRALI
- if TRALI is considered a possible diagnosis, determine donations/donors to be investigated (initially those from female or transfused male donors transfused within 6 hours of onset of TRALI – if these investigations give negative results but TRALI is strongly suspected clinically, investigation should be extended to include donations transfused during the 24 hours prior to the reaction)
- withdraw and / or recall other components from same donation
- temporarily suspend the donor(s) pending investigation results

7. Samples

The NBS laboratory investigations for TRALI are shared between the local H&I laboratory and the national GI laboratory at NBS Bristol. The investigations aim to identify the presence of leucocyte antibodies (HLA class I, HLA class II, HNA in the patient and implicated donor samples. If leucocyte alloantibodies are detected then appropriate tests for the presence/absence of the antigen or allele in the patient/donor will be performed.

It is important to note that there is a possibility of finding donors with HLA or HNA antibodies by chance. It is therefore essential that investigations should determine whether the patient is positive for the cognate antigen. Even if this is the case, the observed incompatibility may have nothing to do with the clinical picture as many patients, who may be positive for the cognate antigen, are transfused with leucocyte antibodies and TRALI does not ensue. The limited diagnostic specificity of the immuno-serological investigations should be taken into account when reporting. The interpretation of the laboratory results must be in the context of a well-documented clinical case history.

7.1 - patient

14 ml clotted and 14 ml EDTA blood samples should be obtained from the patient for:
1. investigation for HLA class I & class II & HNA antibodies
2. HLA and HNA typing as indicated by serological findings.

If a weak leucocyte antibody is found at this stage, it may be either an immune antibody or a passively transferred antibody from the donation. A 20ml follow up clotted blood sample may be required to clarify.

7.2 – donor(s)

Donor samples are required for investigation for the presence of HLA & HNA antibodies and for defining HLA and HNA antigens if required. The latter can only be performed if fresh donor samples are obtained as donor DNA is not routinely archived. The ideal samples are 14 ml fresh clotted and 7 ml EDTA blood obtained from the donor.

If many donors have been identified as possibly implicated then it may be simpler to first screen the archived serum samples from these donors for leucocyte antibodies. Although false positive reactions can be obtained the number of donors which do not require re-sampling can be reduced significantly thus reducing the amount of time it will require to resolve the case. Any positive result from an archived serum sample should be confirmed on a fresh donor sample (14 ml clotted and 7 ml EDTA).

As leucocyte antibodies are produced as a result of pregnancy or transfusion, it is pragmatic to investigate only female donors, and male donors with a history of transfusion, initially. A recent survey of donors has shown that 10-15% of NBS donors have a history of transfusion but no official records are kept on PULSE on the transfusion history of donors. Therefore obtaining reliable information on the donors' transfusion history can be laborious. It is left to the consultant's discretion to decide whether all male donors should be tested or only those with a transfusion history. It should be taken into account that a complete leucocyte antibody screen (HLA & HNA) costs over £300 and a phone call to the donor only 30 p and some consultant time. If leucocyte antibodies are found in a donor and a specificity can be assigned then it is recommended that the relevant HLA and/or HNA genotyping should be performed as indicated using the aforementioned EDTA sample from the donor.

To crossmatch or not to crossmatch

It is logistically complex to perform a lymphocyte and granulocyte cross match.

No cross match
If leucocyte antibodies with an obvious allo-specificity are detected in a donor sample and the patient tests positive for the cognate allele or alloantigen then a cross match is not required.

Crossmatch
Sometimes HLA or other leucocyte antibodies are detected to which no clear specificity can be assigned. In such cases, a crossmatch of donor serum with recipient leucocytes should be performed to confirm incompatibility. A fresh 20 ml EDTA blood sample will need to be obtained once the recipient has recovered from the acute phase of TRALI (returned to normal ward, without assisted ventilation) and after all the donor samples have been collected at the testing laboratory. A sample from the patient should be sent to the Granulocyte Immunology Laboratory in Bristol and must arrive there within 24 hours of sampling. (Note that transfusion within the previous 10 days is a contraindication to performing crossmatch studies because leucocytes can become activated following transfusions).

8. Reporting Of Results

All results on patient and donor samples will be collated on HITS. A single report will be prepared in three sections, the H&I scientific part, the GI scientific part and the medical conclusion/advice part. The final version of the report will be signed by the H&I / GI consultant and reported to the referring consultant, with copies to Lead Consultants and Scientists in H&I and GI, and SHOT.

The report should be generated on HITS using the PGI reporting module as this allows the writing of A4 letter format reports with follow-up sheets if required. The report should be brief, concise and clear. It should summarise the findings of the investigation and indicate whether, on the basis of the laboratory findings (and clinical data if available) the diagnosis of TRALI is:

- Highly likely
  - Donor leucocyte alloantibody with assigned specificity and patient positive for cognate antigen
- Likely
  - Donor leucocyte antibody, no specificity assigned, crossmatch positive or donor leucocyte antibody with incompatibility within a pooled platelet concentrate.
- Possible
  - 1. Patient positive for leucocyte alloantibody with assigned specificity, one (or more) of the donors positive for the cognate antigen. (This scenario is however considered less likely to cause TRALI since all donations are now leucodepleted);
  - 2. Donor(s) positive for leucocyte antibodies with assigned specificity but patient negative for cognate antigen;
  - 3. Weak positive leucocyte antibody without an allele restricted reaction pattern (pan-reactive) and without specificity assigned.
- Unlikely – No leucocyte antibodies in patient and donors

Copies of laboratory reports pertaining to the investigation of the patient's (but not donors') samples should be appended if considered appropriate.

9. Management of Donors

The management of the donors should be linked with the above results categories:

- Highly likely and likely – resign donors positive for leucocyte antibodies with corresponding antigen present in recipients.
- Possible and Unlikely – do not resign donors.

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10. Subsequent transfusion management of patients diagnosed with TRALI

There is no good evidence on which to base transfusion support policy for patients who have experienced TRALI. However, the hypothesis that there may be patient factors which contribute to the risk of TRALI is generally accepted. Based on this reasonable assumption it makes sense to try to avoid further transfusion during the period of illness following the reaction if at all possible. If this is unavoidable, it may be possible to reduce the risk of recurrence by avoiding the use of plasma containing blood components (FFP and platelet concentrates) with a high chance of positivity for leucocyte antibodies, i.e. from female donors. (NBS Issues Departments can provide components from male donors on request of a Consultant.)

The evidence that biologically active lipids play a causal role in TRALI is limited and insufficient to warrant the avoidance of cellular components stored for more that 10 days.

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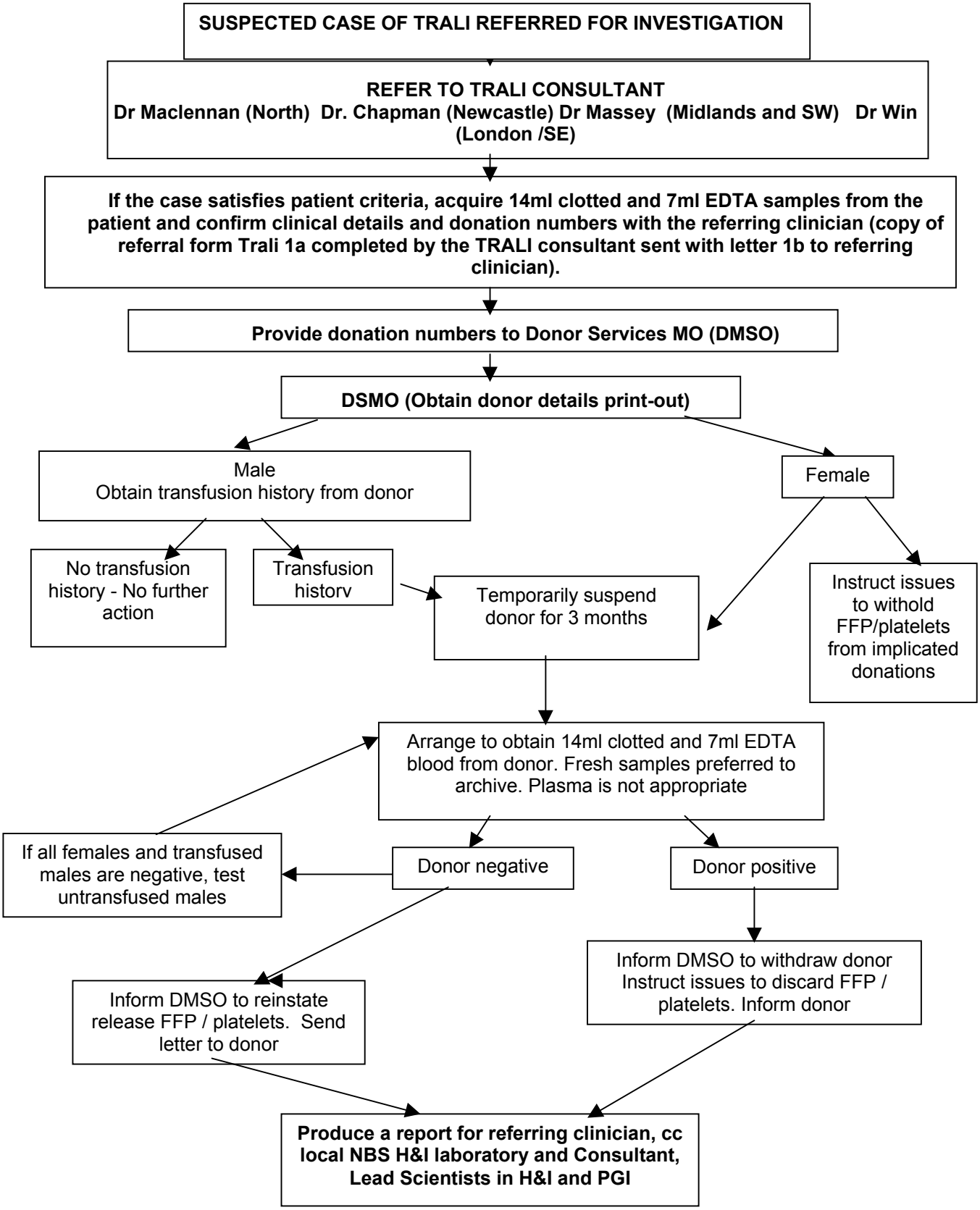
PROCEDURE FOR MANAGING COMMUNICATIONS, SAMPLES AND BLOOD COMPONENTS FOLLOWING REFERRAL OF A SUSPECTED CASE OF TRALI



Appendix

Key to evidence statements and grades of recommendations

The definitions of the types of evidence and the grading of recommendations used in this guideline originate from the US Agency for Health Care Policy and Research and are set out in the following tables.

STATEMENTS OF EVIDENCE

Ia Evidence obtained from meta-analysis of randomised controlled trials.

Ib Evidence obtained from at least one randomised controlled trial.

IIa Evidence obtained from at least one well-designed controlled study without randomisation.

IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.

III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.

IV Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

GRADES OF RECOMMENDATIONS

A **Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation.**
(Evidence levels Ia, Ib)

B **Requires the available of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.**
(Evidence levels IIa, IIb, III)

C **Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality.**
(Evidence level IV)

Summary of ANNUAL REPORT 2001 – 2002

Published 17th July, 2003

Writing Group

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Key Observations and Recommendations

Change in reporting year

➢ With effect from 2003 the SHOT reporting year becomes January to December in line with other major confidential enquiries. This report therefore covers a transitional period of 15 months, and data from October 2001 to December 2002 are included. Where comparisons are desirable with statistics from the previous report the figures are either quoted separately or are adjusted for the unequal time periods.

Participation and number of reports

➢ In 2001–2002 378/405 (93%) eligible hospitals participated in the SHOT scheme. However the number of hospitals submitting reports fell slightly (46%, compared with 48% last year). Nevertheless the overall number of reports received in the period from October 2001 to September 2002 was increased by 15.2% compared with the preceding 12 month period, suggesting that reporting mechanisms are improving in the 'active' hospitals. It is of concern that 191/378 (50.5%) of 'participating' hospitals stated that they had seen no incidents, strongly suggesting that incidents are passing unrecognised or unreported.

Incorrect blood component transfused ("wrong blood") incidents (figure 2)

➢ This category again represents the highest proportion (71.7%) of all of reports received. For the 12 month period from October 2001 to September 2002, 258 new initial reports were received, and a total of 343 to the end of the new reporting year, a 21.1% increase over the equivalent 12 month reporting period 2000-2001. This continuing steep rise in IBCT reports suggests a significant degree of underreporting in the past and increasing awareness and confidence in the SHOT scheme. A real increase in numbers of errors cannot however be excluded.

➢ Multiple errors are a consistent feature of 'wrong blood' incidents, with multiple errors in 137 (40%) of cases. Errors continue to occur at all stages of the transfusion process; 26.9% errors in 39% of case reports occurred at the blood sampling, request and prescription stage; 28.4% errors in 35% of cases took place in the hospital transfusion laboratory; 42.7% errors in 45.9% case reports related to collection of blood from hospital storage sites and bedside administration. By far the most common error 103/552; (18.7%), was failure of the bedside checking procedure, which occurred in 30% of all IBCT cases.

➢ Errors originating in the hospital transfusion laboratory may not be detectable further down the transfusion chain, whilst in other cases a correctly performed bedside check would have averted an incident. Of the 157 laboratory errors, 30 (25%) were grouping errors, 24 (20%) were errors in selection/issue of components, 23 (19.1%) were failure to access the patient's laboratory record, hence failing to meet special requirements. The remaining 80 errors included sample transpositions, missed antibodies or incompatibilities, labelling and other clerical errors, failure to provide irradiated components and issue of outdated blood due to failure to clear satellite refrigerators.

➢ The outcomes of errors reported this year were 32 instances of major ABO incompatible transfusion, resulting in 2 possibly transfusion-related deaths and 4 cases of major morbidity. There were 19 cases of RhD incompatibility (13/19 of these errors originated in the laboratory), of which 3 involved females of child-bearing potential, one of whom is known to have developed anti-D. Eighteen cases of other red cell antigen incompatibilities were reported, 1 of which led to major morbidity. Twenty one patients received unnecessary transfusions because of spurious FBC or coagulation screen results, possibly contributing to 2 deaths. Two patients suffered major morbidity due to ABO incompatible fresh frozen plasma (FFP) infusions.

➢ In 83 cases special transfusion requirements were not met; 60 of these were patients at risk of transfusion-associated graft-versus-host disease who did not receive irradiated cellular components. A particular concern was poor communication, contributing to failures in 20 cases.

"Near Miss" events (figure 3)

➢ This year 146/405 hospitals (36%) reported "near-misses", an increase of 7% from last year. There was a 15% increase in numbers of reports received. Again, sample errors were the largest group; (59%), emphasising the risk of patient misidentification at an early stage in the transfusion process as well as at the end. Medical staff were implicated in 59.6% of these errors. There were 42 (6%) request errors, 87 (12%) errors in laboratory handling and/or testing and 91 cases (13%) of error in the selection, handling and storage of components, of which 27/91 related to incorrect storage in clinical areas resulting in wastage. Errors in component issue, transportation, collection from hospital storage sites and administration accounted for 73 (10%) of cases reported. Reporting of "near-miss" events to SHOT is gaining momentum, but is still at a low level.

Immune complications of transfusion

- There was a large increase in the number of reports of transfusion-related acute lung injury (TRALI) this year with a total of 33 completed reports, of which three were brought forward from last year, and four came between October and January i.e. the additional 3 months of reporting. There were thus 26 new cases in the 12-month period 01/10/01 to 30/09/02, compared with 15 in the corresponding period last year. The diagnosis of TRALI was considered to be highly likely or probable in 18/33 cases, whilst 14/33 were considered possibly TRALI and 1 unlikely. The previously noted preponderance of patients with TRALI who were transfused because of haematological malignancy was not a feature this year, the majority of transfusions (14/33) being for surgical indications.
- The majority of patients with TRALI (21/33) subsequently made a full recovery. One patient was reported to have recovered but with impaired respiratory function. Eleven patients died, 4/11 from their underlying condition whilst in 7/11 death was considered to be definitely (1), probably (2) or possibly (4) due to the transfusion. Assessment of cases of TRALI, particularly retrospectively, is fraught with uncertainties, nevertheless with 7 deaths and 18 cases of major morbidity this year this is emerging as the most important serious complication of transfusion.
- The component most commonly associated with the development of TRALI was FFP (12 cases) with a combination of components in 11 cases, platelets alone in 5 cases and red cells in 5 cases.
- Forty-eight cases of acute transfusion reaction (ATR) were analysed; FFP, platelets or a combination of both were implicated in 31/48 and accounted for 27/34 (79%) of allergic or anaphylactic reactions. FFP continues to be used without good clinical indication. Cumulative data showed that ATR to FFP were 4 times more frequent, proportional to the number of units transfused, than those due to red cells (see chapter 6).
- A newly recognised adverse reaction, that of transfusion-related neutropenia, was reported this year.
- Delayed transfusion reactions (DTR) occurred in 47 patients, and were associated with 3 deaths, 2 definitely and 1 probably due to the transfusion. One further patient suffered severe morbidity. Kidd and/or c antibodies were implicated in 75% of all cases and in all 3 deaths.
- There were no new cases of transfusion-associated graft-versus-host disease (TA-GVHD) this year, and only 3 cases of post-transfusion purpura (PTP), lending further support to the likelihood that quality controlled leucodepletion of all blood components, may partially protect against this complication.

Transfusion-transmitted infections (TTI)

- Between 01/10/2001 and 31/12/2002, 34 post-transfusion infections (PTIs) were reported by blood centres in the UK, 20.9% fewer than in the previous year despite the extended reporting period. Of these, 5/34 cases were confirmed as transfusion-transmitted infections (TTIs) due to bacterial contaminations; the remainder were considered not to have been caused by transfusion or investigations were inconclusive.
- All cases of TTI due to bacterial contamination were caused by platelets, which were 5 days old in 4/5 cases and 3 days old in 1/5. In 3/5 cases the implicated organism was *Staphylococcus epidermidis.* All 5 recipients had major morbidity, and none died.
- Since infection surveillance began in 1995, bacterial contamination has accounted for 26/40 (65%) of TTI incidents affecting 26/43 (60.4%) of infected recipients and responsible for 6/7 deaths. Platelets were implicated in 22/26 cases and *Staphylococcus epidermidis* was isolated in 8/22 cases. The platelets were 3 or more days old in 21/22 cases.
- The absence of any reports this year of transfusion transmitted HCV (or HIV) infections is consistent with the expected low risk of an HCV infectious donation entering the blood supply in the presence of the current testing of blood donations for both anti-HCV and HCV RNA (and anti-HIV).

MAIN RECOMMENDATIONS BASED ON FINDINGS

GENERAL RECOMMENDATIONS

1. All institutions where blood transfusions are administered must participate in SHOT.
Participation in SHOT, already recommended by the UK health departments, will become a legal requirement when EC Directive 2002/98 on Safety of Human Blood becomes UK law. SHOT, which is the UK Haemovigilance scheme, is a driving force for essential improvements in safety for patients who receive blood transfusions. Participation is an essential component of clinical quality and, as recommended by HSC 2002/009 should form part of assessment by regulatory bodies (the Commission for Health Improvement (CHI) and its successor in England and Wales and NHS Quality Improvement Scotland).
Reporting must be timely and should include notification of "near-misses" as well as serious adverse events related to blood transfusion. It is only by highlighting failures that we can learn from them and change unsafe practices. Whilst many hospitals may be investigating "near-miss" incidents internally, we are losing opportunities to learn from each other if we fail to capture and disseminate this information.

2. An open learning and improvement culture must be developed in which SHOT reporting is a key element.
Development of a culture in which the emphasis is on learning from errors in blood transfusion is key to participation in SHOT. Fear of criticism or disciplinary action and uncertainty about the consequences of reporting blood transfusion errors leads to underreporting. This results in lost opportunities to learn from errors and help staff to improve practice.

3. Adequate resources must be made available for improvements in transfusion safety in hospitals.
Commissioners of healthcare (e.g. Primary Care Trusts and Strategic Health Authorities) should ensure that adequate resources are made available to hospitals to allow implementation of the recommendations in this report. They should take an active role in the setting and monitoring of quality standards for blood transfusion.

4. Hospital transfusion teams must be established and supported.
As recommended in HSC 2002/009, hospitals involved in blood transfusion must establish and support a Transfusion Team. As a minimum this comprises a lead consultant in blood transfusion (with dedicated sessions), a hospital transfusion practitioner (nurse, biomedical scientist or medical professional), and the blood bank manager. Chief executives should ensure that the team has full clerical, technical and IT support, and access to audit and training resources.

5. SHOT recommendations must be on the clinical governance agenda.
Hospital clinical governance committees must consider the recommendations contained in SHOT reports and determine an appropriate action plan for improving the safety of administration of blood components within their organisation.

6. Appropriate use of blood components must be strenuously promoted.
Appropriate use of blood is an integral part of any blood safety strategy and should be monitored by regular audit. Concise clinical guidance on the use of blood components is provided by the UK Blood Transfusion Services Joint Professional Advisory Committee and freely available on www.transfusionguidelines.org.uk and as the Handbook of Transfusion Medicine. This guidance is revised in accordance with the current BCSH guidelines. There is a need for continued efforts to ensure that practitioners and patients have ready access to up-to-date, simple, consistent and user-friendly information on best practice.

The finding that 50% of IBCT events occur 'out-of-hours' should be of concern to all hospitals, and transfusions should only take place at night if essential.

7. Training in blood administration should be implemented and competency testing developed to ensure an effective outcome.

The British Committee for Standards in Haematology (BCSH) guidelines on the administration of blood transfusion provide a basis for training in blood handling.

All hospital staff who contribute to the transfusion chain must receive training in the procedures that they are required to undertake and their competency should be formally assessed and recorded.

Professional organisations should work towards development of a nationally accepted and validated system of competency testing for staff involved in the handling and administration of blood components.

8. Blood transfusion should only be prescribed by authorized clinicians.

Blood transfusion should only be prescribed by clinicians who have been authorized by the Trust following appropriate training.

9. Blood transfusion teaching must be included in all relevant academic curricula.

Teaching on blood transfusion safety must be a formal and required part of nursing and medical undergraduate courses and biomedical scientist training. Blood transfusion medicine, best practice and blood safety should be included in the curriculum for medical professional examinations.

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

This year about 35% of blood transfusion errors originated in the laboratory and 31.2% of laboratory errors occurred 'out-of-hours' when laboratory staffing may be sub-optimal. Hospitals should ensure that blood transfusion laboratories have adequate numbers of appropriately trained biomedical scientists to cover the 24-hour working day, including a core of permanent blood transfusion laboratory staff.

Standard-setting bodies need to develop standards for laboratory staffing, both within and outside normal working hours, taking into account pressures such as the requirement for a 4 hour patient turnaround in A & E. Inspection for laboratory accreditation should include the quality of all aspects of the service including 'out-of-hours'.

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

Information technology has enormous potential to reduce the risk of transfusion errors. However, a coordinated approach to the development / assessment of new technologies is needed to ensure quality and "connectability" with other key systems used in the hospital such as patient administration systems, electronic records and systems used in Pharmacy and other clinical areas where positive patient ID is critical. This should be organised at national level. The Chief Medical Officer's National Transfusion Committee in England has recently set up an IT Working Group whose first objective is to bring together the disparate agencies and projects developing clinical IT systems in the NHS. New technologies have the potential to overcome inevitable human error but need to be developed and tested in "real life" clinical environments to demonstrate their true value.

- Electronic positive patient/blood component identification "from vein to vein" using readily available barcode technology and wireless hand-held scanners is already undergoing field trials in the UK. In addition to improving transfusion safety, this technology has many other potential applications in the clinical setting which should increase its affordability. The same electronic ID systems could be used to reduce prescribing and drug administration errors (a considerably greater cause of morbidity and mortality than transfusion errors) and ensure correct attribution of pathology results, dietary regimens and surgical procedures. A coordinated approach is essential to avoid the nightmare scenario of multiple, incompatible, bespoke systems for transfusion, pharmacy, pathology etc in each clinical area.
- Automated laboratory equipment with electronic interfacing reduces the risk of manual transcription and transposition errors but should complement, not replace, skilled and experienced staff.
- Electronic issue of blood from the laboratory without conventional serological "crossmatching" has the potential to improve blood utilization within a hospital and allow laboratories to meet increasing clinical workloads whilst maintaining patient safety. However, secure sample identification and recording of blood group/antibody screen results absolutely essential. Ideally, electronic sample ID and a high level of automated testing, with electronic data transfer, should be used in laboratories using "electronic issue". The standards and specifications of such systems should be clearly defined in authoritative national guidelines which are regularly reviewed to keep up-to-date with technical developments.
- Electronic control of the release of blood components from Blood Banks and satellite refrigerators can improve patient safety and ensure the traceability of blood units. Computer controlled systems with positive patient and product ID, preferably based on barcode reading, can protect patients from one of the most common root causes of mismatch transfusion errors identified in sequential SHOT Reports – collecting the wrong unit from the refrigerator. These systems can also monitor the location and storage status of blood throughout the hospital and improve the traceability of blood as required by the new EU directive. They will be particularly valuable where a central blood bank serves several geographically remote sites or a large number of satellite refrigerators. Once again, these systems should be developed and tested in routine clinical practice to ensure utility and robustness under normal working conditions.

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

Each SHOT report contains specific recommendations. However SHOT has no authority over implementation and cannot monitor compliance. Decision-making pathways are needed to enable data from SHOT to influence blood safety policy.

Bodies which support research, development and health technology assessment should consider blood safety and alternatives to transfusion when setting their funding priorities.

13. Poor communication is an important cause of adverse events.

Clear policies must be developed for communicating special transfusion needs of patients to other hospitals or units which may share their care, so as to ensure that all pertinent transfusion history is available. This is particularly relevant to peripheral blood and bone marrow stem cell transplant recipients. Active involvement of patients in this aspect of their care could reduce the frequency of errors and adverse reactions.

Increasing use of fludarabine means that many more patients are susceptible to TA-GVHD. Pharmacy departments should play a role in notifying patients and hospital blood banks when this therapy is commenced. The forthcoming BCSH guidelines on the avoidance of Transfusion Associated GVHD (which extend the current guidelines for irradiation) include advice on communication where there is shared care and include input from the Pharmacists/Pharmacologists community.

SPECIFIC RECOMMENDATIONS

Incorrect component transfused

- **SHOT recommendations should be used locally to support risk management, clinical governance and education.**
    - In order for patients and staff to derive full benefit from the SHOT scheme, local initiatives to disseminate the main messages of the SHOT report are essential. These could form part of induction sessions for all staff groups or be regular sessions at hospital "Grand Rounds" or departmental training programmes.
    - Reporting should be the norm and full investigation of reported incidents should be carried out by individuals who are familiar with good practice guidelines for transfusion. SHOT findings should be part of mandatory training for all staff involved in the transfusion process.
    - All staff should be made aware through the Risk Management Committee of transfusion errors occurring in their department and in other departments within the hospital. This should not reveal the identities of individuals concerned, the emphasis being on avoiding repetition of errors and encouraging staff to analyse their working practices to identify potential "weak links" which can be remedied.

- **Improved training of midwives in relation to anti-D administration is necessary**.
    - There is increasing risk of mis-administration with the rolling out of the routine antenatal prophylaxis programme. More secure and explicit communication of antenatal and postnatal results is required.

- **Human error in relation to patient identification is still the commonest problem leading to wrong-blood-in-patient.**
    - Educational initiatives have been inadequate in resolving this problem. Patients should be empowered to be involved in the bedside checking procedure.
    - Investment in the development and evaluation of technological solutions is essential if errors in the transfusion process are to be significantly reduced.

"Near Miss" events

- Patients should wherever possible be educated about their own special transfusion requirements.
- Hospital protocols must state that there are no exceptions to the requirement for identity wristbands to be worn by all patients.
- As recommended last year, all hospitals must have a training programme in place for phlebotomy which must include medical staff.

Immune complications of transfusion

- **Patients receiving transfusion must be monitored.**
    - Patients receiving any blood component must be monitored to detect an acute reaction. Patients must be checked prior to the transfusion of each component and 15 minutes after its commencement.

- **Reduction of the risk of TRALI demands a high priority**.
    - Hospitals should continue to be aware of TRALI and to investigate and report possible cases. Continued education of all staff about this condition is encouraged so that cases may be investigated appropriately and implicated donors withdrawn.
    - Following evaluation of available options (e.g. sourcing of FFP from untransfused male donors, suspension of platelets in plasma-free medium), UK Transfusion Services should take all steps possible to reduce the risk of TRALI from blood components.

- **All adverse reactions should be fully investigated and reviewed**.
    - Analysis of cases of acute transfusion reaction and TRALI was unsatisfactory as many cases were not fully investigated and clinical details were sketchy. It is recommended that there is early evaluation of cases by the consultant(s) involved. A team approach including the haematologist and chest physician and/or ITU consultant may be helpful. The blood services are refining the algorithm for investigation of TRALI so the laboratory investigation of cases should in future be more consistent and complete.
    - Patients who have had a severe allergic reaction (anaphylactic/anaphylactoid) should be investigated for IgA deficiency.
    - There is a need for a guideline dealing with the investigation of all acute transfusion reactions.
    - A system of open, non-anonymised reporting to SHOT and specialist review of cases would improve evaluation of the risk of TRALI and should be developed.

- **FFP continues to be associated with significant risks of reactions including TRALI.**
    - FFP should only be used when clinically indicated in accordance with BCSH guidelines. It is particularly important that guidelines for the management of high International Normalised Ratios (INRs) due to warfarin therapy are also followed.
    - There is continued evidence of inappropriate use of clinical FFP and further local audits and educational programmes should be encouraged. A revised BCSH guideline is expected during 2003; in the meantime, existing BCSH guidelines should be followed.

- **Particular care should be taken when providing blood for patients with a positive direct antiglobulin test (DAT), who are known to have an autoimmune haemolytic anaemia or have been recently transfused.**
    - Referral to a reference centre, if time allows, should be considered.
    - Where plasma samples are routinely used for pre-transfusion testing, it is recommended that serum samples are also used in the investigation of suspected transfusion reactions.

- **Suspected delayed haemolytic transfusion reaction should be carefully investigated.**
    - Investigation should include retesting of the pre-transfusion sample by different or more sensitive techniques. This may involve referral to a reference centre.
    - Serum (+ plasma if used routinely) should preferentially be used, to give maximum potential for identifying all antibody specificities present, including weak complement binding antibodies.

- **Patients with sickle cell disease (SCD) should be phenotyped prior to transfusion and blood selected for Rh and K.**

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

- **Information on previous transfusion history must be available to all who need it.**
    - Consideration should be given to issuing antibody cards to all patients with clinically significant red cell antibodies.

These should be accompanied by 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 cross-matched for surgery.
- When the care of patients with haematological disorders requiring transfusion support is shared, there is a risk that not all pertinent transfusion history will be available to both sites. In the absence of networked pathology information systems, it is essential that local procedures are devised for adequate communication.

- **Withholding transfusion may be a greater risk than DTR.**
  - When the laboratory cannot supply compatible red cells within the time-frame requested, there should be communication between the haematologist and the responsible clinician to determine whether the risk of delaying the transfusion outweighs the risk of a transfusion reaction and whether potentially incompatible red cells should be given.

- **No cases of TA-GVHD this year, but risk remains of this fatal consequence of transfusion.**

  - Despite the lack of cases this year, hospitals should remain aware of TA-GVHD and should be rigorous in putting systems in place to ensure that all patients at risk receive gamma irradiated products.
  - Products where partial haplotype sharing is likely should be irradiated. If donor lymphocytes are homozygous for one of the patient's haplotypes the donor lymphocytes can survive. Because they do not share the other haplotype of the patient, however, they can recognise the patient as foreign and set up a GVHD reaction. This is particularly likely to happen if HLA matched products or products from family members are used and for this reason these products should always be irradiated.
  - New chemo- or immuno- therapeutic regimes should be assessed for their potential to cause TA-GVHD and guidelines modified accordingly.

- **PTP is a rare but treatable consequence of transfusion.**

  - Clinicians should remain aware of this rare but treatable consequence of transfusion. The mainstay of treatment is high dose intravenous gammaglobulins +/- steroids, with random (i.e. unmatched) blood components given only if there is significant bleeding.
  - If PTP is suspected, there should be urgent liaison with a reference laboratory for appropriate specialist investigation.
  - PTP is induced by a re-exposure to HPA antigen in individuals with a history of previous immunising events. PTP can therefore occur following transfusion with any platelet-containing product. Now that leucodepletion removes most platelets from red cell components it may be that the classic picture of PTP occurring after red cell transfusion will change and we will see proportionately more cases following platelet transfusion. Non-classical cases should be reported to SHOT.
  - Patients with HPA antibodies should have appropriate antigen-negative cellular products if they require transfusion in the future. Screening should be offered to female relatives of child-bearing potential to see if they are at risk of forming antibodies capable of causing fetal/neonatal alloimmune thrombocytopenia. For HPA-1a this would include HLA typing for HLA DR 101 to identify those who are likely to form antibodies.

Transfusion-transmitted infections

- **Transfusion-transmitted bacterial infection remains an avoidable cause of death and major morbidity and merits increased efforts to prevent bacterial contamination of blood components.**

  - These include implementation of diversion of the first few mL of the donation (likely to contain any organisms entering the collection needle from the venepuncture site) and improvements in cleansing of donors' arms. Methods for testing platelets for bacterial contamination should be evaluated.
  - The risk of transfusion of a contaminated component can be reduced by adherence to BCSH guidelines with regard to the visual inspection of units for any irregular appearance immediately prior to transfusion (particularly platelets).
  - Hospitals should consult the blood service about the investigation of transfusion reactions suspected to be due to bacteria. National guidance on the investigation of these cases are available from all NBS centres. Cases that are inconclusive due to discard of the implicated pack before sampling continue to be reported, therefore particular attention should be paid to the sampling and storage of implicated units.

Neonates and children are a vulnerable group with special transfusion requirements.

- Laboratory, nursing and medical staff should all be aware of the special consideration of component selection and/or manipulation for neonatal transfusion.
- The wearing and checking of patient identification is essential in the paediatric age group, who may not be able to identify themselves verbally.
- Children receiving blood components should be closely monitored.
- BCSH guidelines are as applicable to children as to adults and should be followed.
- Paediatricians should be encouraged to report suspected transfusion-related adverse events and to disseminate lessons learned.

What is SHOT?

The Serious Hazards of Transfusion (SHOT) Scheme was launched in November 1996, and aims to collect data on serious sequelae of transfusion of blood components, as listed below. Through the participating bodies, SHOT findings can be used to:

a) inform policy within transfusion services
b) improve standards of hospital transfusion practice
c) aid production of clinical guidelines for the use of blood components
d) educate users on transfusion hazards and their prevention

Cases included - The scheme aims to capture data on major complications of transfusion:

Non-infectious

- Incorrect blood component transfused (*even if no harm arises*)
- Acute or delayed transfusion reactions
- Transfusion-associated graft-versus-host-disease
- Transfusion-related acute lung injury
- Post-transfusion purpura
- Autologous pre-deposit incidents

Infectious

- Bacterial contamination
- Post transfusion viral infection
- Other post-transfusion infection e.g. malaria

System for Reporting

Cases are reported in the first instance to the hospital haematologist responsible for transfusion. Non-infectious hazards are then reported confidentially to the National Co-ordinator on a simple report form. This is followed up with a detailed questionnaire. Meaningful data depend on questionnaires being fully completed. Staff may write to the SHOT office under separate cover.

Suspected cases of transfusion-transmitted infection are reported by haematologists through supplying Blood Centres to the National Blood Authority/Health Protection Agency Communicable Disease Surveillance Centre. Local Blood Centre involvement is **ESSENTIAL** to ensure rapid withdrawal of other potentially infected components.

Confidentiality

Data are stored in a password-protected database in a secure location. Once all the information has been gathered about an event and entered onto the database without patient, staff or hospital identifiers, all reporting forms and other paper records which contain any identifiers are shredded. The questionnaires (which have any possible identifiers removed) are kept in a secure container until data analysis for the report is complete after which they are shredded.

SHOT does not provide details of individual cases, or any form of summarised data to any outside person or organisation, other than that provided in the report.

Limitations of the SHOT system

Reporting to the SHOT scheme is voluntary. We acknowledge that many incidents may go unrecognised or unreported, and that the reports analysed cannot provide a full picture of transfusion hazards.

Organisation

SHOT is affiliated to the Royal College of Pathologists. The operational aspects of the scheme are the responsibility of a Standing Working Group, which is accountable to the Steering Group. Two National Co-ordinators (D Stainsby and K Davison) together with an assistant (H Jones) are responsible for receiving and collating reports.

Standing Working Group

Dr D Stainsby (Chair), Mrs H Jones, Mrs D Asher, Ms C Atterbury, Dr H Cohen, Dr D Norfolk, Mr J Revill, Ms K Davison, Dr A Todd, Dr C Beatty, Dr S Knowles, Dr C Taylor, Ms C Milkins

Steering Group

Ownership of the scheme and data generated from it resides with the Steering Group, which has representation from the following Royal Colleges and professional bodies:

British Blood Transfusion Society	*Dr JAJ Barbara*
British Society for Haematology	*Dr H Cohen (Chair)*
Institute of Biomedical Science	*Mr W Chaffe*
	Mr JA Revill
Institute of Health Care Management and NHS Confederation	*Mr I R Cumming*
Health Protection Agency/Communicable Disease Surveillance Centre	*Dr M Ramsay*
Royal College of Anaesthetists	*Dr AJ Mortimer*
Royal College of Nursing	*Ms C Atterbury*
	Ms B Cottam
Royal College of Nursing Midwifery Society	*Ms. P. Edkins*
Royal College of Obstetricians and Gynaecologists	*Dr T Johnston*
Royal College of Pathologists	*Prof M Contreras*
Royal College of Paediatrics and Child Health	*Dr B Gibson*
Royal College of Physicians	*Dr CG Taylor*
Royal College of Surgeons	*Prof JSP Lumley*
UK Transfusion Services	*Dr DBL McClelland*
Blood and Tissue Safety Assurance	*Dr E M Love*
Founding Member	*Dr L Williamson*

Overview of results for this report

The numbers of reports in each category received since the first SHOT annual report are shown below.

Table 1: Adverse events reported during the five reporting years 1996/97 to 2001/02

	1996/1997	1997/1998	1998/1999	1999/2000	2000/2001	2001/2002*
IBCT	81	110	144	201	213	258 (343)
ATR	27	28	34	34	37	38 (49)
DTR	27	24	31	28	40	33 (46)
PTP	11	11	10	5	3	3 (3)
TA-GVHD	4	4	4	0	1	0 (0)
TRALI	11	16	16	19	15	26 (32)
TTI	8	3	9	6	6	5 (5)
Unclassified	0	0	7	0	0	0
TOTAL	**169**	**196**	**255**	**293**	**315**	**363 (478)**

IBCT: Incorrect blood component transfused
ATR: Acute transfusion reaction
DTR: Delayed transfusion reaction
PTP: Post-transfusion purpura
TA-GVHD: Transfusion associated graft-versus-host-disease
TRALI: Transfusion-related acute lung injury
TTI: Transfusion transmitted infection

* The figures in brackets are the total numbers of reports received during the full 15 month period 1st October, 2001 to 31st December, 2002.

Figure 1: Overview of 482 cases for which fully completed questionnaires were received

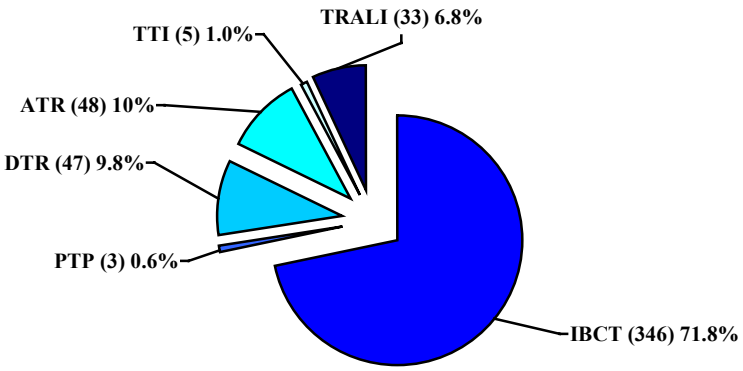


Table 2: Transfusion related mortality/morbidity according to the type of hazard reported in 482 completed questionnaires

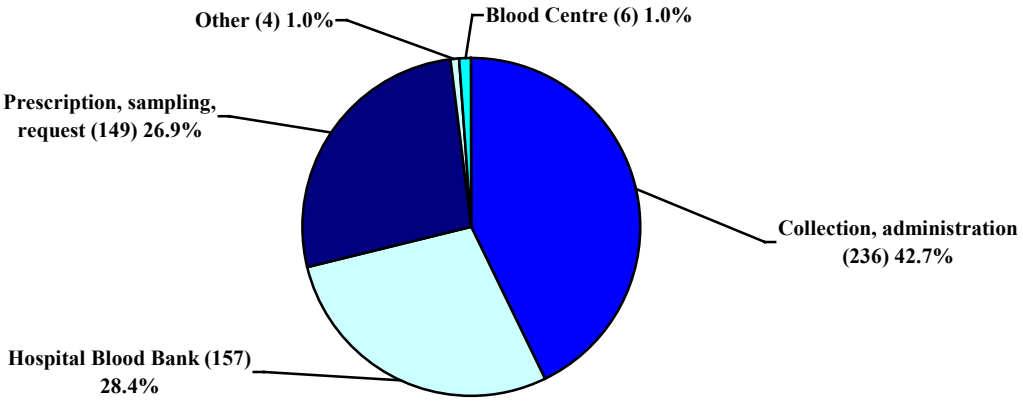
	Total	IBCT	ATR	DTR	PTP	TRALI	TTI
Death definitely attributed to transfusion	**3**	0	0	2	0	1	0
Death probably attributed to transfusion	**5**	1	1	1	0	2	0
Death possibly attributed to transfusion	**8**	3	1	0	0	4	0
Death due to underlying condition	**33**	18	5	6	0	4	0
Major morbidity	**35**	9	0	2	1	18	5
Minor or no morbidity	**393**	310	41	36	2	4	0
Outcome unstated	**5**	5	0	0	0	0	0
Totals	**482**	**346**	**48**	**47**	**3**	**33**	**5**

Major morbidity was defined as the presence of one or more of the following:

- Intensive care admission and/or ventilation
- Dialysis and/or renal dysfunction
- Major haemorrhage from transfusion-induced coagulopathy
- Intravascular haemolysis
- Potential RhD sensitisation in a female of child-bearing potential
- Persistent viral infection
- Acute symptomatic confirmed infection (viral, bacterial or protozoal)

Incorrect Blood Component Transfused

Figure 2: Distribution of total errors according to the main reporting categories (n=552)



Cumulative data from 6 years of SHOT reporting 1996/97 to 2001/02

Figure 4: Questionnaires by incident 1996/97 – 2001/02 (n=1630)

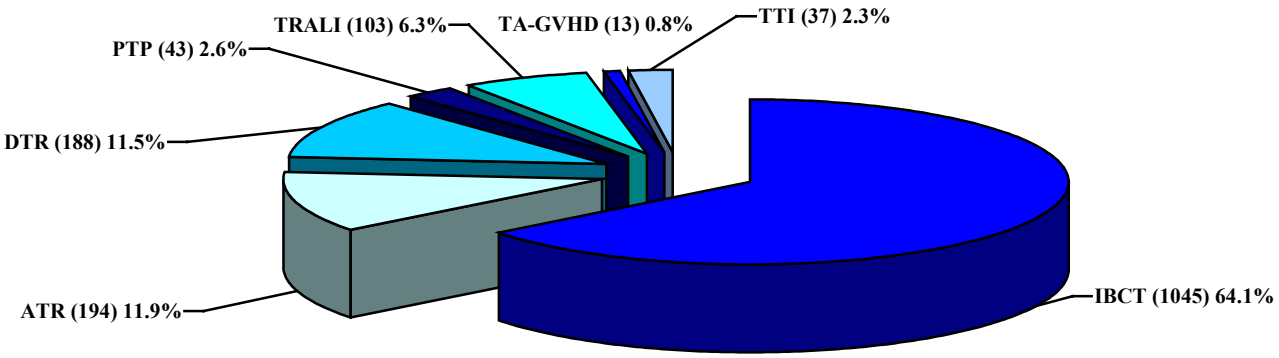
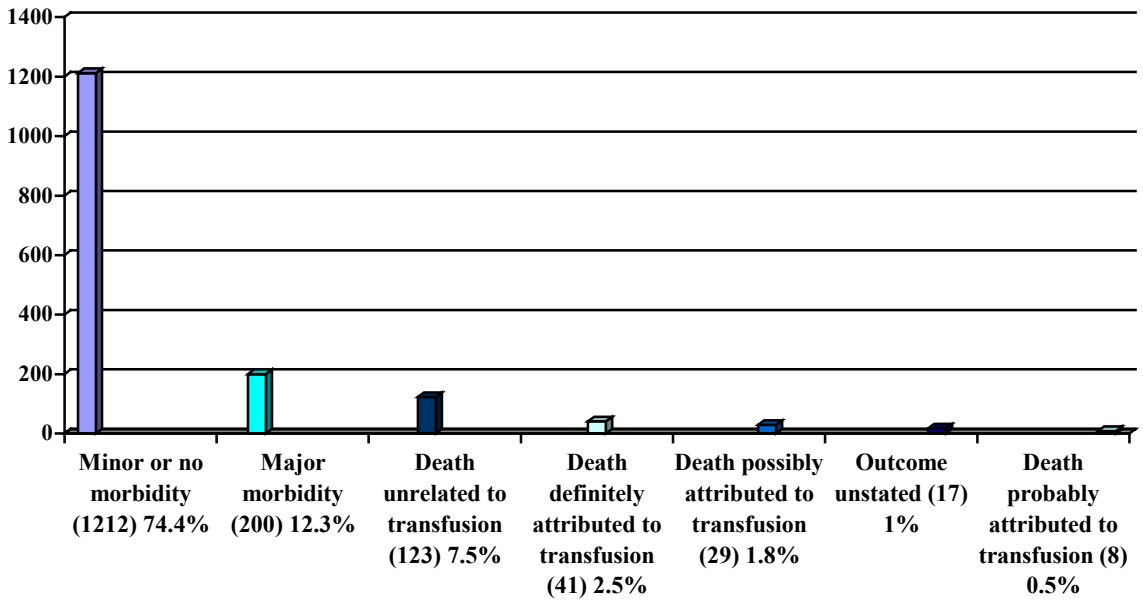


Figure 5: Overall mortality/morbidity figures 1996/97 – 2001/02 (n=1630)



This summary has been sent to hospital haematologists, blood bank managers, and NHS Trust Chief Executives. Copies of the full report (price £25) are available from the SHOT office. Please make cheques payable to National Blood Authority and write 'SHOT' on back of cheque. National Health Service employees are invited to apply to the SHOT office for a free copy of the report.

An electronic copy of the report is available on the SHOT website together with selected presentations from the Symposium on 26th September 2003

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