SERIOUS HAZARDS OF TRANSFUSION

ANNUAL REPORT

1998 - 1999

Affiliated to the Royal College of Pathologists

British Blood Transfusion Society, British Society for Haematology
Faculty of Public Health Medicine, Institute of Biomedical Science
Institute of Health Care Management, NHS Confederation
Public Health Laboratory Service Communicable Disease Surveillance Centre
Royal College of Anaesthetists, Royal College of General Practitioners
Royal College of Nursing, Royal College of Obstetricians and Gynaecologists
Royal College of Paediatrics and Child Health
Royal College of Physicians, Royal College of Surgeons, UK Transfusion Services

Published 7th April, 2000

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ISBN **0 9532 789 2 1**

CONTENTS

APPENDICES

1. Terms of reference and membership of Steering Group and Standing Working Group
2. Income and expenditure statement
3. Initial report form for non-infectious complications
4. 'Nil to report' card
5. CDSC/PHLS report form for infectious complications
6. Near-miss forms
7. Autologous transfusion form and questionnaire
8. Sample questionnaires
    a) Incorrect blood component transfused
    b) Acute transfusion reaction
    c) Delayed transfusion reaction
    d) Transfusion-related acute lung injury
    e) Post-transfusion purpura
    f) Transfusion-associated graft-versus-host disease

GLOSSARY OF TERMS

ATR	Acute transfusion reaction
BCD	Buffy coat derived
BCSH	British Committee for Standards in Haematology
BSH	British Society for Haematology
PHLS/CDSC	Communicable Disease Surveillance Centre of the Public Health Laboratory Service
CMV	Cytomegalovirus
CPA	Clinical Pathology Accreditation
DAT	Direct antiglobulin test
DTR	Delayed transfusion reaction
ELISA	Enzyme-linked immunosorbent assay
FFP	Fresh frozen plasma
HLA	Histocompatibility locus associated
HTC	Hospital transfusion committee
IAT	Indirect antiglobulin test
IBCT	Incorrect blood component transfused
LD	Leucocyte depleted
LISS	Low ionic-strength sodium
MCA	Medicines Control Agency
MSBT	Microbiological Safety of Blood and Tissues Committee of the Department of Health
NBA	National Blood Authority
NBS	National Blood Service
NEQAS	National External Quality Assurance Scheme
NHSE	National Health Service Executive
NICE	National Institute for Clinical Excellence
PTI	Post-transfusion infection
PTP	Post-transfusion purpura
RCP	Royal College of Physicians
RCPath	Royal College of Pathologists
RhD	Rhesus D
TA-GVHD	Transfusion-associated graft-versus-host disease
TRALI	Transfusion-related acute lung injury
TTI	Transfusion-transmitted infection

1. MAIN FINDINGS AND RECOMMENDATIONS

1. Participation

A. Number of hospitals
Of the 432 hospitals eligible to participate, 132 (30.6%) submitted reports, representing an increase of 4% over the previous year and an overall increase of 8.5% since the scheme began in November 1996. A further 204 hospitals sent "Nil to Report" returns. Overall participation is now running at 77.8% (336/432 hospitals), compared with 65% last year. When it is considered that 64.6% of participating hospitals are responsible for 90% of annual red cell usage in the UK and Republic of Ireland, this increase in participation is very gratifying.

B. Number of reports received
A total of 252 reports were received this year, an increase of 27.9% from the 197 new reports last year[1], and an overall increase of 49.1% since the scheme began[2]. As in previous years the largest category remains "incorrect blood component transfused" with 144 reports this year, compared with 110 last year, an increase of 30.9%.

Recommendations

(i) In line with Health Service Circular 19981224 'Better Blood Transfusion'[3], systems of Clinical Governance within Trusts should ensure a commitment to SHOT reporting and to changes in practice resulting from SHOT observations and recommendations.

2. Incorrect blood component transfused ('wrong blood') incidents

A total of 144 cases has been reported (30.9% more than last year), of which receipt of completed questionnaires has enabled analysis in 136. The continued increase in reports of these cases, which is disproportionate compared with the increase in reporting hospitals, is probably due to increased recognition of transfusion complications, although a true increase in the underlying frequency of events cannot be excluded. There were 35 ABO incompatible transfusions (a similar percentage to last year), with 3 deaths, 1 clearly and 2 possibly related to the transfusion. 5 other cases developed clinically significant haemolysis.

For the third year running the most important single cause of mis-transfusion was failure of some aspect of the bedside checking procedure immediately prior to administering the transfusion. Causes included remote checking at the nurses' station or treatment room rather than at the bedside, checking the component against the accompanying paperwork rather than the patient, and failure to note discrepancies between compatibility and donation labels where laboratory labelling errors had occurred. There was some evidence to suggest that interruption during this critical step may have played a significant part in failure of the process.

The withdrawal of the wrong pack from its storage location in the hospital continues to be a common error and, in this report, was always followed by mis-identification at the bedside. The absence of patient identification wristbands or alternative formal means of identification contributed to 15 cases, 7 of which were related to outpatient transfusions.

Although only 2 cases resulted from samples being taken from the wrong patient these errors are important since they may not be detected later in the transfusion process. Both occurred in "classic" settings: confusion between two unknown accident victims and a mix-up over maternal and infant samples. In the latter case pre-labelled tubes were used, contrary to current BCSH guidelines[4].

Laboratory incidents included technical errors, sample transposition and labelling mistakes. Half the laboratory errors occurred "out of hours"; more data are required to ascertain the significance of this finding. There were 15 cases of failure to request the appropriate component, most commonly for patients requiring irradiated components, and several incidents of transfusion of incompatible plasma, as a result of incorrect serological reasoning.

The historical transfusion record was not checked or there was failure to act on relevant information from it in 22 instances. Such errors usually occurred in association with errors in other parts of the transfusion chain. Confusion over telephone messages appeared to be a factor in some errors. Several problems, including an ABO incompatible transfusion, arose in relation to the management of blood stored in satellite refrigerators.

'WRONG BLOOD' INCIDENTS ARE PREVENTABLE.

Recommendations

(ii) An important guideline on how to achieve this has been published by the BCSH (British Committee for Standards in Haematology)[5], but not widely distributed. This guideline, reproduced in Appendix 8, must now be widely disseminated to all staff handling blood. The Hospital Transfusion Committee provides a useful structure through which this can be done.

(iii) Hospitals must ensure that ALL staff handling blood receive correct training and regular retraining.

THE FINAL BEDSIDE CHECK

(iv) The bedside check is the last opportunity to detect an identification error, and it is vital that its importance is recognised. The environment in which the transfusion is conducted must provide adequate working space, and allow staff responsible for the bedside check to carry out an uninterrupted checking procedure.

(v) Hospital systems must ensure that there are no exceptions with regard to the provision of patient identity wristbands or their equivalent. This is particularly important in the outpatient setting where familiarity with the patient may lead to a tendency to cut corners in the formal checking procedure. It is appreciated that a visible patient identity band may be difficult to achieve in theatre, but since it is the only definitive means of identifying an unconscious patient, all possible steps must be taken to maintain visible patient details.

INFORMATION TECHNOLOGY WILL PREVENT HUMAN ERROR

(vi) COMPUTERISED IDENTIFICATION SYSTEMS ARE AVAILABLE TO ENSURE SAFE TRANSFUSION AT THE BEDSIDE. THESE SYSTEMS MUST NOW BE EVALUATED. THE NHS IT STRATEGY SHOULD TAKE A LEAD IN ASSESSING THIS AREA OF NEW TECHNOLOGY.

The above recommendations relate to the final bedside check. However, this will not necessarily detect errors of sampling or errors in the transfusion laboratory, so equal importance must be given to the earlier steps in the transfusion chain.

PREVENTION OF ERRORS IN EARLIER STEPS IN THE TRANSFUSION CHAIN

(vii) Individuals responsible for the prescription and request of blood components must be familiar with the special requirements of their patients. These requirements should conform with BCSH guidelines and must be flagged on the patient's clinical and laboratory records.

(viii) Staff responsible for taking samples for transfusion testing must at all times follow strict procedures to avoid confusion between patients at the time of sampling. Sample tubes must never be pre-labelled and labelling must be completed for one patient before moving on to the next. Special care is required when dealing with "unknown" multiple casualties.

(ix) **The historical transfusion record must be available in the blood bank, consulted and acted upon at all times.** It is an essential tool in ensuring the safety of the transfusion process. Access to information about previous grouping and special requirements may prevent a mis-transfusion.

(x) **Blood banks must continue to be vigilant in reviewing procedures, systems, and training to prevent sample handling and technical errors.** Despite increasing automation and computerisation in hospital laboratories, transfusion testing remains an area where skill as well as training in established procedures is of paramount importance.

(xi) **Hospitals must develop unambiguous protocols for the management of blood in satellite refrigerators**.

(xii) **Telephoned requests for blood components must be formally recorded and include full patient details plus any special transfusion requirements.**

(xiii) **Hospitals must ensure that standards are set for minimum formal identification requirements when blood is collected from the hospital blood bank, and that staff undertaking this procedure are fully trained and aware of the key role which they play.** The correct collection of blood components from the hospital storage location is an essential intermediate step in the transfusion process. Mistakes at this point set the scene for subsequent errors resulting in wrong blood incidents.

3. Immune complications of transfusion

There was a slight increase in reports of acute (34) and delayed (31) reactions, with new reports of transfusion associated graft-versus-host disease (TA-GVHD 3), post-transfusion purpura (PTP 10) and transfusion associated acute lung injury (TRALI 16) remaining at a constant level.

These cases do not generally reflect poor practice. Acute reactions comprise a spectrum of symptoms, overlapping with simple febrile reactions and TRALI. With the exception of haemolytic events, reactions were investigated rather inconsistently, and it was not always possible to determine the cause of the reaction.
There was no clear association between leucodepletion and any specific types of adverse event.

Of the TA-GVHD cases, one was a patient with B cell malignancy (making 5 in 3 years), and 2 cases followed cardiac surgery (making 3 in 3 years). In two initially reported cases, follow up questionnaires were not returned. There were no cases of TA-GVHD due to failure to prescribe irradiated components appropriately, and none in which irradiated components were implicated. However there were 7 episodes in which patients who should have received irradiated blood did not.

PTP is almost certainly underreported, but cases were investigated and managed appropriately. This is the first year in which platelet alloantibodies combined with heparin-associated antibodies have been reported. As many as 50% of patients receiving heparin develop antibodies detectable by ELISA techniques, but ≤ 5% of those develop thrombocytopenia, usually in conjunction with thrombosis[6].

Over 3 years, there have been 43 reported cases of TRALI, following transfusion of red cells and platelets as well as fresh frozen plasma (FFP). Of these, 6 have been fatal, and a further 23 have required ITU care. If all such cases truly had TRALI, this total of 29 cases makes TRALI the second most common cause of transfusion related death/major morbidity exceeded only by ABO incompatibility. However, TRALI may be difficult to diagnose clinically, and not all cases were supported by positive donor serology.

Recommendations

(xiv) Clinicians should continue to report all types of serious adverse event following transfusion, as this may act as an early warning of adverse effects of novel techniques and processes (e.g. leucocyte depletion, virus inactivation, drug/product interactions).

(xv) Symptoms of acute reactions to platelets and FFP may overlap with those of TRALI but this diagnosis cannot be confirmed without appropriate investigations for donor and recipient white cell antibodies. It is recommended that such investigations are performed (via the supplying blood centre) whenever respiratory symptoms are prominent.

(xvi) Laboratories should ensure that appropriate additional cell panels and techniques are employed to exclude potential masking, by known antibody(ies), of previously undetected antibodies. NEQAS (National External Quality Assurance Scheme) can offer a range of technologies which may not be available locally.

(xvii) Any possible impact of universal leucocyte depletion of the blood supply (achieved in November 1999) on TA-GVHD incidence will take several years of further monitoring to emerge, so it is critical that full details of all cases are returned to SHOT. A standard protocol for the investigation of suspected TA-GVHD cases should be developed.

(xviii) Patients at risk of TA-GVHD who are receiving shared care between a transplant/ oncology centre and their referring hospital should carry a card to indicate their need for irradiated components.

(xix) In patients diagnosed as having heparin-induced thrombocytopenia in whom there is no thrombosis, platelet-specific alloantibody investigations should be considered if the patient has ever been pregnant or transfused .

(xx) UK Transfusion Services should consider possible strategies for prevention of TRALI. This recommendation needs to be considered in its broadest aspects, including an option appraisal of different approaches to donor selection/screening, logistics, effect on the blood supply and cost-effectiveness.

4. Transfusion-transmitted infections

Of 34 suspected cases, only 7 were confirmed to be related to transfusion, with a further 17 in which transfusion was eliminated as a source of infection. The 7 cases comprised 1 hepatitis B, 1 hepatitis C and 5 bacterial transmissions, of which 2 were fatal. In both hepatitis cases, detection was because of subsequent illness or positive serology in the donors, neither of whom reported risk factors that would have led to their exclusion from blood donation. Although both recipients were infected, neither had developed acute symptoms: they were tested following positive hepatitis serology in the donors.

Of the 5 bacterial cases, 1 was a fatal *Yersinia entercolitica* transmission from a 33-day old non-leucocyte depleted unit of red cells, 2 were from apheresis platelets (1 *Staphylococcus epidermidis* and 1 *Escherichia coli* (fatal)), and 2 were from pooled platelets (1 *Staph epidermidis* and 1 *Bacillus cereus*). All 4 platelet donations were at least 3 days old.

Several reports have been received of components that were observed to have visual signs of bacterial contamination before use, were not transfused, were sent for bacteriological investigation and were found to contain bacteria expected to cause disease in a recipient if transfused. These reports indicate "near-miss" bacterial transmissions. The investigation of the source of the contamination in these cases can be as informative as the investigation of transmissions, and the possibility of requesting and collating some information about these cases in the future is being considered.

Recommendations

(xxi) Careful inspection of blood components can, in some cases, detect bacterial contamination and prevent potential transmission. Components showing any unusual

colour, turbidity or clumping should not be transfused, but should be returned to the Hospital Blood Bank for culture.

(xxii) Clinicians should report all suspected post-transfusion infections in their patients to the blood service (via their supplying blood centre) for appropriate investigation. Reporting should be done with urgency so that other implicated blood components from the donor can be rapidly withdrawn. Blood centres should, in turn, complete an initial report form for PHLS CDSC as soon as possible.

(xxiii) The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. Hospitals should consult guidelines and the blood service about the investigation of such cases, including the sampling and storage of implicated units. National guidelines (from the NBS) on the investigation of these cases are currently being revised following comments from users.

(xxiv) Donors' clinicians (and donors themselves) should be encouraged to report to the blood service any history of previous blood donation if they are later found to be carrying a transfusion-transmissible infection, in order that follow-up of any potentially infected recipients can be conducted speedily and appropriate care given.

(xxv) National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge.

5. Priority setting in blood safety

This report contains many recommendations which require action at local level. However some proposals require policy decisions taken centrally, either by the UK Transfusion Services or by the Department of Health e.g. allocation of new resource into patient identification systems, strategies for TRALI prevention. The UK still lacks a single strategic framework for blood safety which incorporates all relevant expertise, including that from the specialties of Public Health and Health Economics. This is discussed more fully in Chapter 15.

Recommendation

(xxvi) There remains a need for an overarching approach to decision making in relation to blood safety. A national unified body is needed, with appropriate relevant expertise and representation from professional bodies which can prioritise new initiatives in blood safety. This should be complemented by a parallel initiative on appropriate prescription of blood.

2. FOREWORD - WORKING TOWARDS A CO-ORDINATED NATIONAL APPROACH TO BLOOD SAFETY

With publication of this third Annual Report, the position of SHOT as a respected source of data on transfusion complications in the UK is now firmly established. The number of hospitals participating has increased from 65% in 1997/98 to 78% in 1998/99, and 65% of these are responsible for 90% of all red cell usage, which is highly gratifying for such a young scheme. The NHSE circular 19981224 'Better Blood Transfusion' recommendation that all Trusts participate in SHOT by April 2000 should now encourage universal reporting[3].

In particular, we have drawn attention to the problem of 'wrong blood transfused' incidents which continue to comprise over half the cases reported. Following the first SHOT report, the BCSH developed a very useful guideline on blood administration (Appendix 8). It is essential that this guideline is disseminated widely within Trusts. If used as the basis for a comprehensive staff training (and retraining) programme, this guideline offers sound practical advice on how transfusion errors can be reduced. However, to reduce 'wrong blood' episodes to the vanishingly low level of viral transmission now seen, innovative computing developments to ensure correct blood/patient identity would be required. Such a strategy would require novel patient identification/administration systems in every Trust as has been undertaken in UK Blood Centres. These systems would have other major advantages, e.g. in reducing errors in drug administration. In September 1999, SHOT held a workshop on automated blood/patient identification systems (Chapter 3). Commitment is now needed at Trust Chief Executive level to take this initiative forward and Clinical Governance provides a framework within which such innovation can be given local priority. However, considerable new investment is needed and the NHS IT strategy should take a lead in assessing this area of new technology.

With the introduction of universal leucocyte depletion, and virus inactivated fresh frozen plasma beginning to be prescribed, SHOT has encouraged prescribers to report any type of unusual reaction to transfused components. In this way, SHOT can provide early warning of rare new complications of these novel components. SHOT now includes complications of pre-deposit autologous donation, and will work towards incorporation of complications associated with other autologous transfusion procedures, in collaboration with the Autologous Transfusion Special Interest Group of the British Blood Transfusion Society. This year, SHOT has finally joined the Internet, and you can find us at **http//www.shot.demon.co.uk.**

To maintain the momentum of the first 3 years, we are considering how the setting up of the National Institute for Clinical Excellence (NICE) might facilitate the running of SHOT and implementation of our recommendations. Other UK-wide Confidential Enquiries such as those into peri-operative deaths, maternal deaths and stillbirths/infant deaths are being incorporated into the NICE structure, and we are exploring the possible benefits this might bring for SHOT. It is our firm intention, however, to maintain a professional affiliation with the Royal College of Pathologists.

The 3 SHOT reports together offer a comprehensive picture of transfusion complications in the UK. This provides powerful data against which future priorities for transfusion safety enhancements can be considered. However, as discussed in Chapter 15, this is possible only if combined with a strategy for considering transfusion risks together, and setting priorities for allocation of resources. A national unified body is needed with overall responsibility for blood safety, complemented by a parallel initiative on appropriate prescription of blood.

Hannah Cohen MD FRCP FRCPath
Chair, Serious Hazards of Transfusion (SHOT) Steering Group.

3. WORKSHOP: IMPROVING THE SAFETY OF BLOOD TRANSFUSION AT THE BEDSIDE

Manchester Blood Centre: 30th September, 1999

Following the publication of the first two SHOT annual reports it is clear that, regardless of how many errors may have contributed to the transfusion of an incorrect blood component, the bedside check is a critical opportunity to prevent mistransfusion. There are a number of reasons why this particular aspect of the transfusion process goes wrong albeit relatively rarely. For instance, checking patient details at the nurses' station or other location away from the bedside is common and formal checks are sometimes performed inadequately either because of pressure of work or because of perceived familiarity with the patient.

The idea of organising a workshop specifically designed to widen the debate on these issues came from the SHOT Standing Working Group after publication of the second report. The team felt that there was a need to bring together a group of people from a wide variety of disciplines and with diverse professional interests but for whom the importance of improving the bedside checking process formed a common interest. What we did not anticipate was the intense enthusiasm generated by this initiative which resulted in far more people wanting to participate than was logistically possible. Because of the nature of the workshop — it was intended to be an interactive meeting rather than a conference — we had to restrict the numbers of invitations and we apologise to anyone who may feel that they were missed out. The final guest list included representatives from the fields of haematology, nursing, anaesthetics, laboratory science, trust executive management, risk management, information technology and commercial manufacturers of patient identification systems.

The workshop was split into two sections with an opportunity over lunch to see demonstrations of the products which our commercial delegates manufacture and market. The morning session was devoted to a series of brief lectures designed to give an overview from various perspectives. The afternoon was advertised as a "brain storming" session with the aim of consolidating the diverse aspects of the problem, investigating potential solutions, and deciding how best to proceed.

Morning Session
Chair: Dr. Elizabeth Love

Dr. Love opened the meeting by explaining the reasons for organising the workshop and by expanding on the set objectives for the day. The main objectives were:

1. Define the problem

2. Outline potential solutions

3. Identify obstacles

4. Corporate Strategy

Dr. Mike Murphy, Oxford, the first of our guest speakers, began by defining the sequence of events in the multi-step process which ultimately leads to the transfusion of a blood product. From the initial prescription of a product to the final administration stage the chain of events is long, complex, and inevitably error prone. Despite long standing awareness that wrong blood transfusions occur, no formal system of reporting adverse events existed in the UK prior to the formation of the SHOT scheme. Dr Murphy discussed some of the results of a national survey of blood banks which was carried out by the Edinburgh group in the early 1990s and compared these with the results of the first two years of SHOT reporting.

He went on to describe the state of patient identification systems currently in use. Some non-automated systems of patient identification are already in place in the UK. They have been shown to provide an extra safeguard against bedside errors but still do not prevent a significant number of misidentification incidents taking place. In contrast, automated systems which involve bar coding of products and patient wristbands have proved to be very successful in error prevention where they are in use in some parts of the United States. Although there is widespread support in the UK in principle for bar coding systems there has been little success to date in securing funding for the installation of these systems. In conclusion Dr. Murphy stressed the importance of positive patient identification at the time of both sampling and administration of the product and suggested that education and training will continue to play a vital role in error prevention.

The second speaker, **Dr. Brian McClelland**, **Edinburgh,** introduced the topic of responsibility for errors. A close analysis of all the steps in the transfusion process reveals an immense number of individual activities all of which have the potential to go wrong. The disparate nature of events in the transfusion chain makes the task of ensuring safe delivery of blood products a difficult one to manage. The SHOT reports have shown that errors occur often and that multiple errors frequently contribute to a wrong transfusion. Staff involved in these events include medical officers, porters, laboratory scientists, nurses, receptionists, and orderlies all of whom may have different line managers. This clearly makes an overall management strategy difficult to achieve and may lead to friction and confusion between the various disciplines.

Dr. McClelland asked "Could we do better?" In some parts of the USA it has been shown that it *is* possible to make significant improvements. Better funding and higher levels of litigation may be two of the factors contributing to this situation. It is possible that we may begin to see some positive steps being taken following the implementation of clinical governance in this country but funding will continue to be an issue. Technological solutions are undoubtedly attractive and desirable but are, nonetheless, a long term solution. In the meantime more emphasis needs to be placed on finding interim solutions and targeting those areas, such as collection of a wrong component from the blood bank, which contribute most often to a multi-error event.

Dr. Jeff McIlwain, Whiston Hospital, addressed the meeting on the subject of Risk Management in relation to the transfusion process concentrating largely on the topic of litigation in the UK. In 1995 awards made as a result of claims for medical negligence and special damages amounted to £100 million. Underlying this, 7 times more incidents took place for which no claim was made and 14 times more claims were made than sums awarded. Clearly, any information relating to the cost of litigation does not accurately reflect the scale of the problem.

In seeking compensation for an incorrect component transfused the single most important question to be considered is "was the patient harmed?" Claims of this sort are routinely made under the umbrella of Medical Negligence although awards for negligence are not generally high. For example if blood were to be given to a patient who is a Jehovah's Witness and who stated clearly that this would be against their wishes, the charge would be battery and, if the claim were successful, could result in an award of approximately £2000 plus special damages. In the case of a transfusion of an incorrect component with no resulting adverse sequelae the sum awarded might be similar. The large sums of money awarded which are reported regularly by the press are not usually the result of a negligence claim but constitute compensation in the form of "special damages", for example for such factors such as pain and loss of earnings which can attract high levels of compensation. It seems unlikely that the numbers of claims for compensation will diminish. Indeed, as patients become more knowledgeable and aware, the numbers of cases reaching the courts looks set to rise and it may be advisable for Trusts to weigh the potential costs of such an increase against the cost of funding methods to improve blood safety.

The next three speakers represented commercial companies involved in the marketing of technological solutions to the problem of positive patient identification.

Colin Clark, Immucor Inc. described the product marketed by his company in terms of software, hardware, purpose and benefit. The system effectively removes the need for large quantities of paper work and replaces this with a reliable electronic system of data capture. It utilises state of the art technology and involves scanning bar codes on blood bags, patient wristbands, and notes to ensure the delivery of the right product to the right patient every time. The system has the added benefit of

improving productivity by removing the need for a second nurse to check transfusion details although 'single person' checking is now supported by the BCSH Guideline on blood administration[5]. The system is already in use throughout the USA, and is about to be implemented in Toronto, Canada. Hospitals in Milan have also shown an interest and it is anticipated that installation will take place there in the near future.

Mike Wilks, Symbol Technologies emphasised the desirability and effectiveness of bar code technology and pointed out that the NHS does not recognise the value of such systems. IT systems presently in use in British hospitals have outmoded technologies which do not communicate with each other. It is becoming clear that there is a need for foolproof methods of patient identification and that the relevant technology has already been developed. Trusts should take into account the fact that bar coding systems have numerous applications. Quite apart from the obvious benefits pertaining to safer blood handling, the potential for avoiding errors in drug administration is equally patent. In summary, the technology exists, it is simple to learn, simple to use, and of comparatively low cost.

Lyn Sharman, Datalog International Ltd. outlined the obstacles he has encountered and still encounters in trying to convince hospitals of the wisdom of installing bar code technology. Despite the fact that demonstrations of his system usually provoke an enthusiastic response he has been unable to identify anyone who is willing to take the next logical step of installing the equipment. The major problems are that there is an unwillingness to accept accountability, responsibility and leadership together with an inability to identify funding. One (unnamed) hospital was quoted as saying that patient identification was not a priority. The situation as it stands in this country was described as "a national disaster" with outmoded methods of patient identification such as hand-written wristbands being the norm. Technology itself is not the problem. Bar code technology has been in regular use at our local supermarkets for a long time and is very successful. Some systems can be expensive but others are not and at the very least ought to be seriously evaluated. If one problem can be identified as the ultimate obstacle to progression in this area it is the problem of change management. What is needed if we are to move on is a clear leadership strategy.

Afternoon Session
Chair: Dr. Hannah Cohen, London

Dr Cohen began the afternoon session by introducing the final two guest speakers and explaining the format of the "brain storming" session which would follow.

The first of the afternoon speakers was **Mr. Ian Cumming, Morecambe Bay Hospitals NHS Trust**, who gave an overview of Clinical Governance from the perspective of a Trust Chief Executive. It is now well recognised that: 1) the detection of adverse events in blood transfusion is good; 2) the investigation of adverse events is good; but 3) changing practice as a result of lessons learnt from these events is much more difficult. The situation has not been helped by the formation of hospital Trusts which has resulted in barriers to the dissemination of information.

Chief Executives have the responsibility to put systems in place which can detect errors and subsequently correct them. It is important that this is not in any sense a blame process. Clinical Governance is concerned with clinical quality and involves not only staff but systems and equipment. Staff need to be constantly evaluated for competence, performance and educational needs. None of this is new, but all the things which Clinical Governance is responsible for need to come together. This system of evaluation is standard in other industries but not, for the moment, in the NHS. A comparison is often made between the role of airline pilots and anaesthetists because they have been shown to have very similar psychological profiles. Consider the following:

Table 1
Comparing Airline Pilots with Anaesthetists

Airline Pilots	Anaesthetists
Every 6 months required to have a full medical (whole day)	No equivalent conditions or requirements exist for anaesthetists
Every 6 months required to undertake a simulator test	
Every year to be assessed while flying	
At any time may be required to be accompanied by an observer	
Not permitted to fly more than 900 hours per year or 100 hours per month	
Not permitted to fly different models of aircraft without prior training	

These are the kinds of standards we ought to expect for NHS staff. Clinical Governance came into being largely as a result of the much publicised events which took place in Bristol and which served to undermine public confidence. To reiterate: Clinical Governance is about quality and its focus needs to be on education, systems, and processes.

The final speaker of the day was **Professor Alastair Bellingham**, **Chair of the new NHS IT Special Health Authority,** who outlined the NHS IT strategy. The present government has identified poor IT communication as one of the most significant factors in the delivery of a poor service and has stressed that a proper communication strategy needs to be introduced. A measure of the importance which the government is attaching to this is to be found in the substantial sums of money which are being ring fenced for the project.

There is a seven year agenda designed to address some common problems. Currently patients are given a different hospital number for each hospital they attend, GP systems are stand-alone and don't communicate with each other; NBA and PHLS systems are good, but they need to be able to link with each other. One of the first changes to be implemented will be the new NHS numbering system which will be used to identify patients regardless of which hospital they are admitted to. This system will be 100% operational very soon and should eliminate the problem of patients carrying more than one hospital number. In theory this will provide hospitals with the ability to obtain medical information about a patient whenever and wherever it is needed.

Brainstorming Session
Leader: Dr. David Gozzard, The Glan Clwyd Hospital

Dr Gozzard commenced this workshop session by recapping on the earlier lectures and then invited participation from the floor.

One of the first suggestions was that it might be beneficial to run a pilot trial of one or more of the bar coding systems which had been demonstrated during the morning. A discussion followed about what would constitute a suitable area for such a pilot. The suggestions ranged from a children's unit (since this would provide a small and, therefore, affordable area) to an area which experiences high levels of stress (in order to stretch the system to its limit). A number of potential difficulties were identified, however, including the need to have some baseline data before any pilot could realistically take place. One delegate suggested that there may be some baseline data available in one hospital from the results of an audit which took place following publication of the SHOT report. Another obstacle to a pilot was identified as the need to agree on a definition of a near miss event since near misses are far more frequent than adverse events. Perhaps the greatest problem with running a pilot is one of interpretation of the results. Incorrect components transfused are comparatively rare events and a short pilot on a small unit may well not capture a single episode. Inevitably that would mean that the pilot may appear to be successful (by 'proving' that the new technology works) but still prove impossible to roll out because of the unreliability of the data.

It was suggested that there are other projects which might be undertaken which do not necessarily involve a technological solution. For example we do not currently have any data on levels of

compliance with guidelines or policies. One delegate advised that putting a person on the ground to observe this phenomenon would not be difficult and that observation of as few as 100 transfusion episodes would be enough to show a non-compliant trend. The point was also made that a reduction in the numbers of transfusions carried out would probably contribute to reduction in adverse events and that this would make an interesting audit in itself. The idea of undertaking audits or studies of aspects of the problem which do not involve the implementation of additional technology is one which is attractive to budget holders. Part of the difficulty which managers have in trying to allocate resources lies in the fact that serious transfusion errors are rare and there is a perception that money would be better spent on direct patient care.

During a wide-ranging discussion, it was agreed that this constitutes a huge area and, while much of the discussion had been focused on technological solutions, it should not be forgotten that these would be unlikely to be implemented quickly. Therefore there needs to be constant reinforcement of the importance of continuing education, training, and improvements to documentation. The implementation of the new international blood bank barcode standard ISBT 128 also has an impact on this area and it was agreed that SHOT should be kept appraised of new developments from the UKBTS/NIBSC Standing Advisory Committee on Information Technology.

It was generally agreed that the day had been useful and that it should provide the impetus to move forward. The formation of a smaller group to develop pilot studies of the new technology seemed to offer the best solution and Dr. Gozzard was invited to form just such a group reporting to the Standing Working Group.

4. 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. Since the launch of the first Annual Report, SHOT has received widespread and very positive coverage both within the UK and overseas. The following are national and international meetings during 1998 and 1999 in which members of the SHOT team have participated in order to present the work of SHOT.

1998

March :	• European Commission Workshop on Haemovigilance, Luxembourg
April :	• British Society for Haematology Annual Scientific Meeting, Glasgow • Institute of Biomedical Scientists Blood Group Serology Conference, Durham • International Biomedical Science Symposium, Ireland
May :	• 5th NATO Blood Conference, Lisbon
June:	• Royal College of Nursing Forum, York
July:	• International Society of Blood Transfusion Scientific Meeting, Oslo
July:	• UK Chief Medical Officers' Symposium on Evidence-Based Blood Transfusion
September:	• British Blood Transfusion Society Annual Scientific Meeting, Nottingham • Institute of Biomedical Sciences Scientific Meeting
November:	• Royal College of Pathologists Transfusion Update Meeting • Autologous Transfusion 3 years on, Royal College of Physicians of Edinburgh

1999

January:	• National Haemovigilance Meeting, Athens
March:	• RCN Congress, Harrogate

April:	• Transfusion Nurses Forum, Edinburgh • British Society for Haematology Annual Scientific Meeting, Brighton
May:	• Blood Transfusion in the Surgical Patient: Lessons from the SHOT reporting system, University of Liverpool • BBTS Technology SIG, Aston University, Birmingham • The SHOT reporting scheme, Spanish Blood Transfusion Society, Madrid
June:	• Scottish Society of Anaesthetists, Conference Centre, Stirling • 'Crises in Haematology' Meeting, Royal College of Pathologists, London • National (Canadian) Transfusion-Transmitted Surveillance System Steering Committee Meeting/CJD Planning Meeting, Winnipeg, Canada
September:	• BBTS Annual Scientific Meeting, Edinburgh • De Securité Transfusionelle et d'Haemovigilance, Lille
October:	• Advancing Laboratory Practice in Haematology, Guernsey
November:	• Launch of the Haemovigilance Scheme for the Republic of Ireland, Royal College of Surgeons, Dublin • Trasfusione Sicura: la prevenzione dell errore in reparto: Haemovigilance in the UK, Milan • Vertrouwd en Vernieuwend: Haemovigilance in the UK, Utrecht • 'Resuscitation Fluids: State of the Art', Royal College of Surgeons, London

In addition, Dr Lorna Williamson is co-chair with Dr Luc Noel, World Health Organisation, Geneva of a Working Party on Haemovigilance on behalf of the International Society of Blood Transfusion.

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- Williamson LM, Lowe S, Love E, Cohen H, Soldan K, McClelland DBL, Skacel P, Barbara JAJ. The Serious Hazards of Transfusion Annual Report 1996-1997, ISBN 09532 789 0 5, 18th March 1998
- Williamson LM, Lowe S, Love E, Cohen H, Soldan K, McClelland DBL, Norfolk DR, Revill J, Barbara JAJ, Birrell D, Todd A. The Serious Hazards of Transfusion Annual Report 1997-1998, ISBN 0 9532 789 1 3, 9th March, 1999

Abstracts

- Williamson LM, Love E, Lowe S et al for the SHOT Steering Group. UK Serious Hazards of Transfusion (SHOT) initiative - results from the first year of reporting, Vox Sanguinis, 74/S1/98
- Cohen H, Love E, Williamson L. Serious Hazards of Transfusion (SHOT), Crises in Haematology meeting June, 1999. The Bulletin of the Royal College of Pathologists; Abstracts Section, 1999, 108:111
- Cohen H, Love E, Lowe, S, Williamson L, on behalf of the SHOT Steering Group. Serious Hazards of Transfusion (SHOT) Scheme: The Second Annual Report 1997-98 Br J Haematol 1999: 105:suppl 1:30;13
- Cohen H, Love E, Williamson L. Haemovigilance in the UK : serious hazards of transfusion (SHOT). III^{EME} Congres National de Securité Transfusionnelle et d'Hemovigilance. Conference Proceedings 44
- Cohen H, Love E, Williamson L. Serious hazards of transfusion (SHOT) and blood safety. Clin Lab Haematol 1999:21:4-5

5. 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. A recent welcome addition is a representative from the Institute of 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.

The first three years' funding has come from the Transfusion Services within the United Kingdom and Ireland. Generous grants from the British Blood Transfusion Society and British Society for Haematology are gratefully acknowledged. An income and expenditure statement is presented at Appendix 2. Future funding arrangements are currently under discussion although no formal arrangements have been agreed at the time of going to press.

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 and Republic of Ireland, as well as public hospitals in Guernsey, Jersey and the Isle of Man are invited to report.

SHOT invites reports of major adverse events surrounding the transfusion of single or small pool blood components supplied by Transfusion Centres (red cells, platelets, fresh frozen plasma, 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 Control Agency. 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 also 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

Reporting of transfusion-transmitted infections

Suspected cases of transfusion-transmitted infection 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/Public Health Laboratory Service Communicable Disease Surveillance Centre (NBA/PHLS CDSC) post-transfusion infection surveillance system. If the SHOT office is notified directly of an infectious hazard, the hospital haematologist and transfusion centre are approached by the co-ordinator to ensure that all relevant personnel have been informed and that the incident has been reported to NBA/PHLS CDSC.

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 (see Fig 1).

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

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 Northern Zone 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.

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. Whilst the questionnaires seek a full picture of each reported transfusion hazard, a critical appraisal is not undertaken by the SHOT co-ordinators with respect to imputibility i.e. to say whether an incident is attributable to the transfusion. However, those completing the questionnaires are asked to state their opinion on the presumed cause of the incident and, this year, we have asked reporters of fatal cases to assess the imputibility of the transfusion to the death.

'Nil to Report' Card

Due to the anonymity of the scheme, denominator data from reporting hospitals was not provided in the first report. To ascertain the percentage of hospitals contributing to the SHOT reporting scheme in subsequent years, a 'Nil to Report' card and covering letter was sent to the named consultant haematologist at all hospitals held on the SHOT mailing list (424 in 1997/1998 and 432 in 1998/1999). The consultant haematologist was asked if he/she had reported any adverse events to SHOT during the period 01/10/98 to 30/09/99 or, if no adverse events had been seen, to return the card as 'nothing to report'.

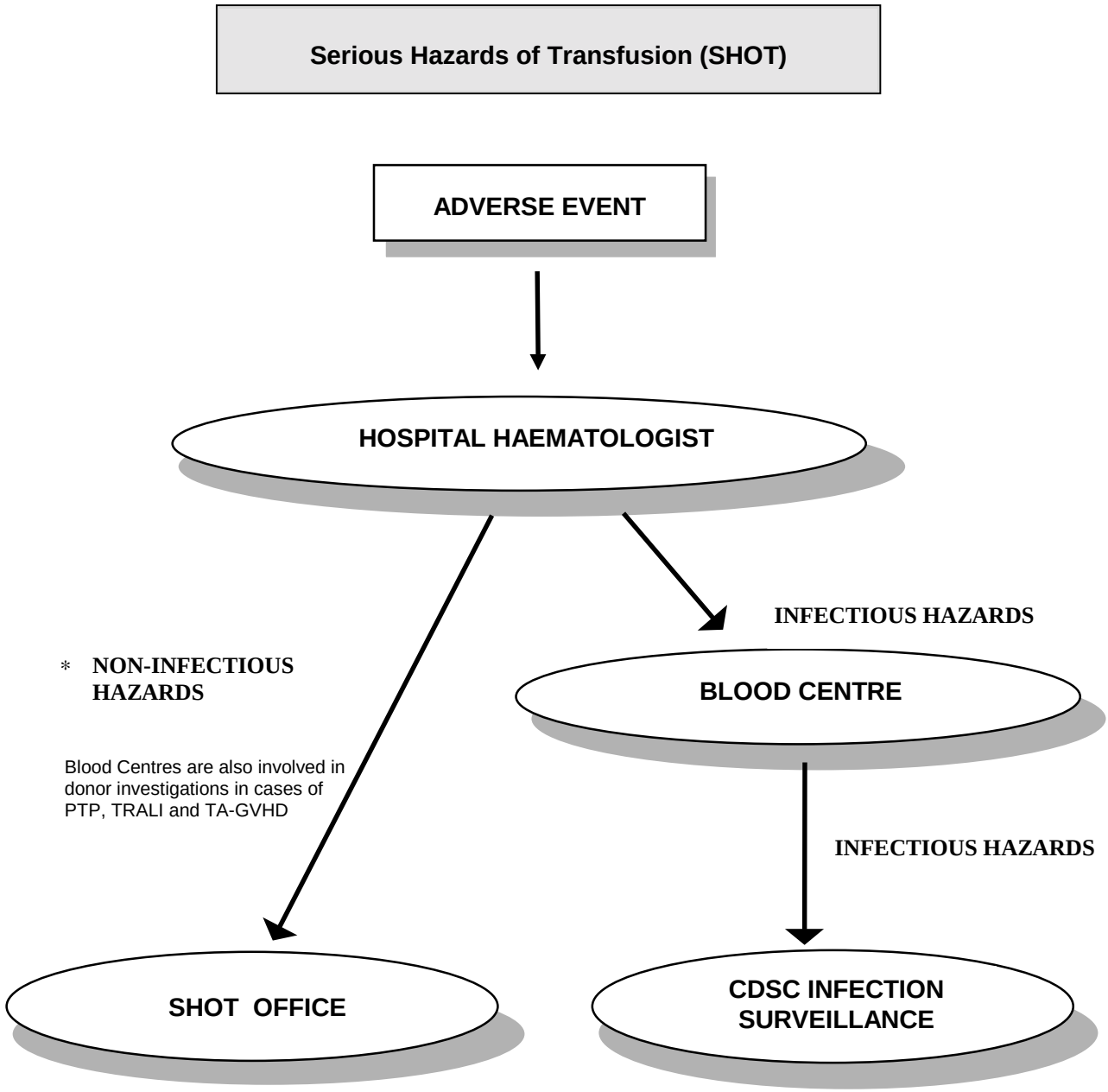
In an attempt to provide a denominator against which transfusion risk could be assessed, we also requested information on the number of red cell units transfused per annum from hospitals sending either reports or 'Nil to Report' cards. This card was also used to ask the hospital if it would like to receive a SHOT receipt as proof of participation in the scheme. For this purpose an address label containing the hospital name and address was provided. On returning the 'Nil to Report' card, hospitals requiring a receipt also returned the address label which was then used to send a receipt. No records were kept by the SHOT office concerning receipts and, once data from the report cards had been entered onto an anonymised spreadsheet, the cards were shredded.

We intend to repeat this exercise annually to keep all hospitals informed of the latest initiatives in the SHOT reporting scheme and to prompt them to report any adverse events. The results of this exercise are detailed in Chapter 6.

Dissemination of results

Approximately 1500 full reports and 2500 summaries are printed annually and distributed, free of charge, to hospital haematologists and medical laboratory scientific officers in charge of hospital blood banks, chairs of professional bodies and others involved in the practice of blood transfusion. In addition summaries are sent to Trust Chief Executives. A small charge is made for full reports sent to non-NHS agencies and individuals.

Figure 1
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

6. OVERVIEW OF RESULTS

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.

The SHOT reporting scheme for non-infectious complications of transfusion was launched on 18th November 1996. After the publication of the first annual report it was evident that there would always be retrospective reporting and a delay in the return of completed questionnaires. For the second SHOT report (1997/98) we chose to analyse data by date of initial report rather than by date of incident. This resulted in some 'double counting' of reports received during 1996/97; for 1997/98 both new and total cases are shown below. This system continues to be used for the current 1998/99 SHOT report which, therefore, includes all initial report forms received between the 1st October 1998 and 30th September 1999.

Overview of reports and "Nil to Report" cards

Number of hospitals

Of the 432 hospitals eligible to participate, 132 (30.6%) submitted initial reports during the reporting year. 103 of these hospitals confirmed that they had previously submitted a report when they returned the "Nil to Report" card. The 132 reporting hospitals represents an increase of 4% over the previous year and an overall increase of 8.5% since the scheme began. A further 204 hospitals sent "Nil to Report" returns. Combining these 204 with the 132 hospitals which sent reports, participation is now running at 77.8% (336/432 hospitals), compared with 65% last year. This increase in participation is very gratifying. 194 (57%) hospitals requested a receipt as proof of participation.

Number of reports

This reporting year showed an increase in reporting of 27.9% (252 initial reports compared with 197 in the previous year). As in previous years the largest category remains "incorrect blood component transfused" with 144 reports received this year. The numbers of reports in each category received since the first SHOT annual report are shown in Table 2.

Table 2
Events reported during the three reporting years 1996 to 1999

		1997/1998		
	1996/97	New Cases	Total	1998/1999
IBCT	81	110	121	144
ATR	27	28	30	34
DTR	27	24	27	31
PTP	11	11	13	10
TA-GVHD	4	4	4	3
TRALI	11	16	16	16
TTI	8	4	4	7
Unclassified *				7
TOTAL	169	197	215	252

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

*****Unclassified = 7 reports which we were unable to categorise. These are discussed separately.

Figure 2 Comparison of incidents reported in 1996/97, 1997/98, and 1998/99

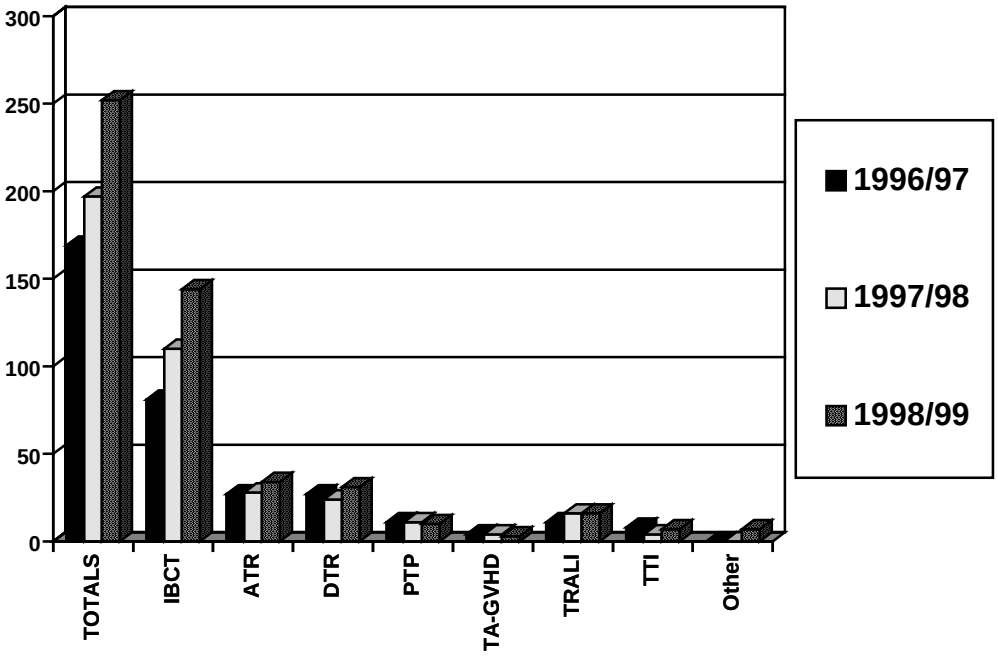
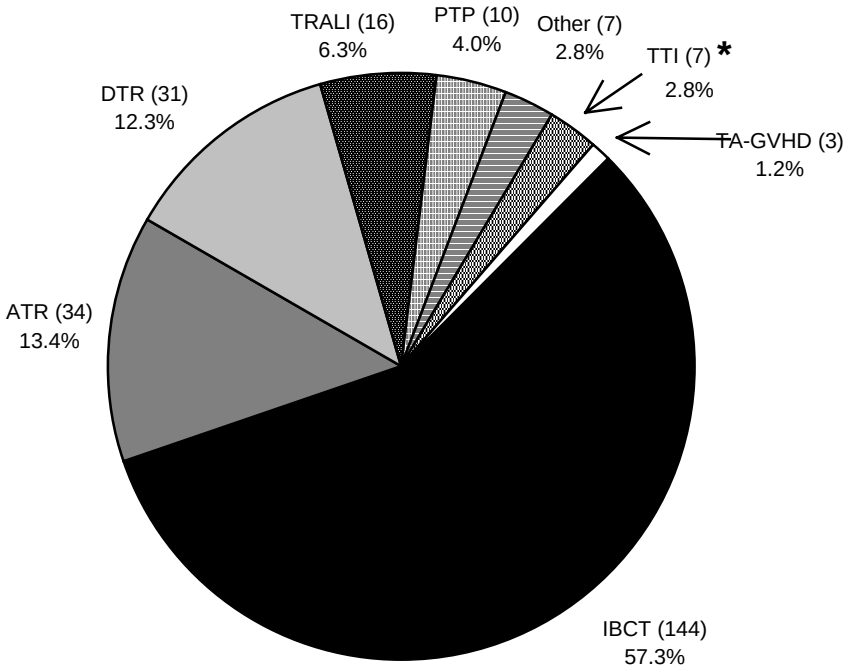


Figure 3 Overview of 252 cases for which initial reports forms were received.



***** Additionally, by another reporting mechanism, 1 probable transfusion-transmitted bacteraemia was recorded in Scotland

Analysis of questionnaires

A total of 235 questionnaires plus 9 explanatory letters were analysed for this report (Total = 244). Included are 12 which were outstanding from the previous year. A further 21 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 20 initial report forms for which no questionnaires were received. 8 of these were eventually closed without analysis because sufficient information could not be obtained.

Table 3
Summary of completed questionnaires received.

	IBCT	ATR	DTR	PTP	TA-GVHD	TRALI	TTI	Unclass-ified	Totals
Total number of reports received	144	34	31	10	3	16	7	7	252
Questionnaires included in analysis	136 (5)	34 (2)	30 (1)	11 (2)	3 (1)	16 (1)	7	7	244
Questionnaires outstanding	13	2	2	1	2	1	0	0	21

These figures include questionnaires outstanding from last year shown in brackets

Figure 4
Overview of transfusion related mortality / morbidity data reported in 244 completed questionnaires.

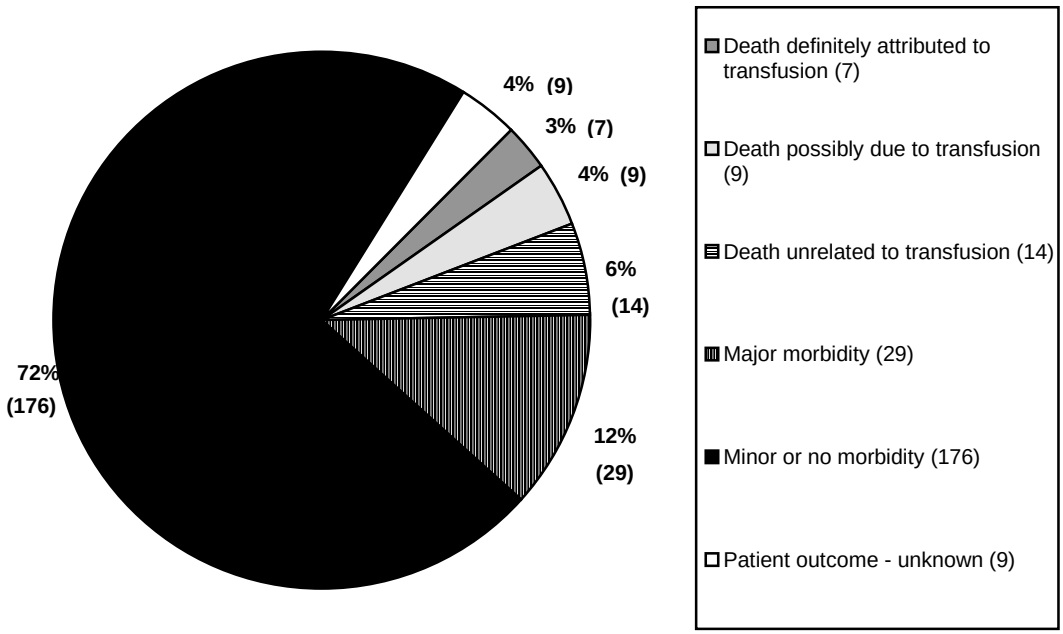


Table 4

Transfusion related mortality/morbidity according to the type of hazard reported in 244 completed questionnaires.

	Total	IBCT	ATR	DTR	PTP	TA-GVHD	TRALI	TTI	Unclass-ified
Death definitely attributed to transfusion	7	1	0	1	0	3	0	2	0
Death possibly attributed to transfusion	9	2	2	0	1	0	4	0	0
Death due to underlying condition	15	10	1	2	1	0	0	1	0
Major morbidity	30	12	1	1	0	0	12	4	0
Minor or no morbidity	175	108	27	26	9	0	0	0	5
Patient outcome - unknown	8	3	3	0	0	0	0	0	2
Totals	**244**	**136**	**34**	**30**	**11**	**3**	**16**	**7**	**7**

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 5
Calendar days between transfusion incident and initial report to SHOT (n=227)

Excludes 7 TTI reports for which the reporting system is different, 7 "Unclassified" cases which will be analysed separately and 3 reports where the date of transfusion was not stated or not known.

The median time for return of initial reports was 17 days compared with 15 in 1997/98 and 30 in 1996/97

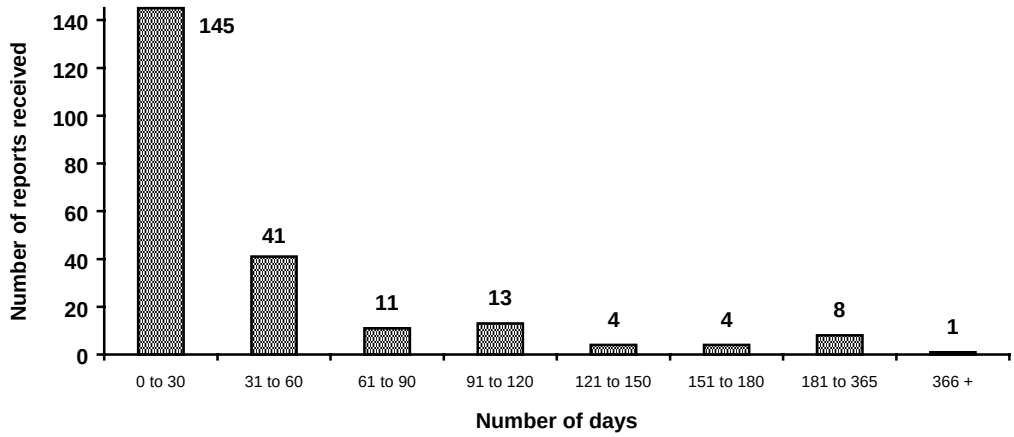
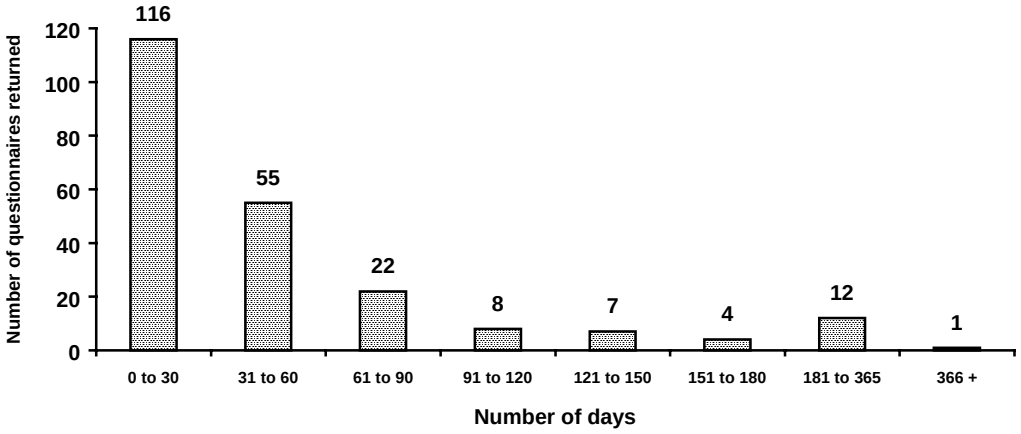


Figure 6

Calendar days between initial report and return of completed questionnaire (n =225)

Excludes 7 TTI, 7 "Unclassified", 4 reported by letter and 1 for which no information is available

The median time between initial report and return of final questionnaire was 19 days in 1997/98 and 49 days in 1996/97. The median time for the current year is 29 days but this figure may be artificially high due to technical problems experienced in the SHOT office during March 1999.



Overall transfusion activity and patient characteristics

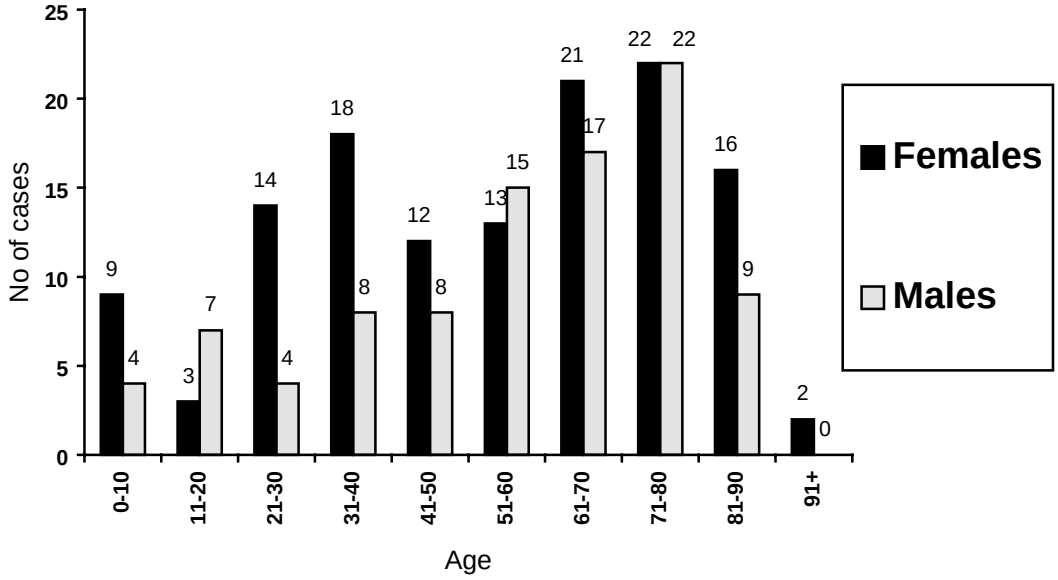
The number of incidents reported needs to be placed in context of the overall numbers of transfusions taking place. Table 5 gives details of total blood component issues from the Transfusion Services in the UK and Ireland. This information represents components issued during the fiscal year 1st April, 1998 to 31st March, 1999

Table 5
Total issues of blood components from the Transfusion Services of the UK and Ireland in 1998/99.

Red cells	2,386,475
Platelets	259,025
Fresh frozen plasma	372,510
Cryoprecipitate	84,218

The "Nil to Report" cards asked hospitals to state how many red cell units were transfused annually. Of the 309 hospitals who returned cards, 279 gave figures for units transfused which totalled 2,140,254 i.e. 64.6% of hospitals eligible to participate receive and handle 90% of all red cell units issued to hospitals. This suggests comprehensive coverage of transfusion hazards.

Figure 7
Distribution of patients by age and sex at the time of transfusion (n=224)



Excludes 6 cases where age or date of transfusion was not stated, 7 TTI, and 7 "Unclassified"

	Females (130)	**Males (94)**
Age unknown	2	1
Date of transfusion not stated	1	2
Age range	0 days to 94 years	29 days to 88 years
Median age	58 years	62 years

"Unclassified" reports received

7 reports were received which could not be categorised using the existing SHOT definitions of adverse events but which, nevertheless, highlight some important risk factors and therefore merit discussion. The reports involved 4 males, 2 females, and one report of 9 units of red cells being transfused for which we have no data relating to the individual recipients.

3 of the cases referred to prolonged transfusion. In 2 of these episodes, the patient developed chest pain during a routine transfusion which was then temporarily stopped. In one such case the transfusion was re-started at normal rate and in the other the rate was considerably slowed down. Both of these cases resulted in the transfusion of red cells which had been at room temperature for a prolonged period (14 ¼ hours in one instance). The third of these incidents occurred when a cannula became blocked shortly after the transfusion started. The cannula remained in situ for over four hours before being re-sited. This patient suffered shivers and mild pyrexia.

1 report was received in which there was calcium contamination of the line which caused clotting in a unit of buffy coat depleted red cells in SAGM. The patient suffered no ill effects.

There was one report which involved a total of 120 units of red cells which were stored at an incorrect temperature during transport between the blood centre and hospital blood bank. The error was discovered on the return of the van to the depot. Subsequent investigation revealed that a small visible warning light in the van was missed by the driver and the audible alarm had been disconnected some time earlier. The hospital was contacted and asked to withdraw all these units which had been exposed to a temperature of >10°C for at least 4 hours. Unfortunately 9 units had already been transfused and one was withdrawn from the patient's bedside. None of the patients who received these units suffered any ill effects. This event would also have been reported as a quality incident at the local blood centre in accordance with the blood service's quality assurance system.

One report was received which stated that a unit of red cells had been transfused approximately 15 hours after its expiry date. The patient suffered no ill effects and although this case was followed up by the SHOT office no further information could be obtained.

The final case involved a transfusion, in an emergency, of FFP to a 23 year old Jehovah's Witness who was in renal failure. The patient had been transferred from elsewhere and normal notes for him were not available. Nursing staff quickly realised the error and the transfusion was stopped before the patient had received 50 ml of FFP. It was not clear how the error was discovered although this hospital has now changed its ward policy so that patients transferred from another location may not be transfused without the full notes being available. They also recommend that Jehovah's Witnesses should have a note attached to the outside of their notes informing staff of their religious affiliation.

Hospital Transfusion Committees

From information obtained from a hospital questionnaire conducted in 1999 by the UKBTS/NIBSC Joint Guidelines Committee's Standing Advisory Committee on Information Technology it is known that of 317 hospitals responding to the question "Does your hospital have a hospital transfusion committee?", 84.5% said they had one, 14.8% said they did not and 2 hospitals did not answer the question.

7. INCORRECT BLOOD COMPONENT TRANSFUSED

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

As in previous years this category represents the highest number of reports (144 or 57.1% of 252 new cases). This chapter analyses 132 questionnaires plus 4 explanatory letters totalling 136 cases including 5 outstanding from the previous reporting year.

In total, 149 initial report forms were received during the reporting period but 5 were not valid SHOT reports and will not be included in this chapter. Table 6 gives a breakdown of these excluded cases.

Table 6
Excluded cases

1	Was considered to be a near miss event
1	Was withdrawn by the reporter
1	Was a duplicate of an earlier report
1	Was considered to be an acute transfusion reaction
1	Was considered to be a clinical decision rather than an error
5	
144	Valid initial report forms
13	Questionnaires are outstanding and will be analysed next year
131	Questionnaires/ letters plus **5** from last year are analysed in this chapter. **Total = 136**

Sex of recipients

Females	76
Males	60

Age of recipients

Age range	0 days to 94 years
Median Age	59 years

Components Implicated	Number of Cases
Red cells	112
Platelets	11
Fresh Frozen Plasma	5
Cryoprecipitate	2
Cryo poor plasma	1
* Anti-D immunoglobulin	5

* Adverse events to this plasma product are usually reported through the MCA yellow card system, but they are reported here because they fall into the category of either blood derivative to the wrong patient or as a result of RhD typing errors.

Table 7
Outcome of 136 fully reported incidents

Outcome	Number of incidents
Death definitely related to transfusion	1
Death possibly related to transfusion	2
Death unrelated to transfusion	10
Major morbidity*	12[1]
Survived with no ill effects	108
** Unknown	3

[1] includes 5 cases recovered from complications of intravascular haemolysis

*Major morbidity was classified 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 risk of RhD sensitisation in a female of child-bearing potential

** 3 cases had outcomes unknown at the time of reporting. 1 patient had been referred to another hospital and 1 was still receiving dialysis. In a third case the reporter stated that it had been difficult to obtain co-operation from the relevant consultant.

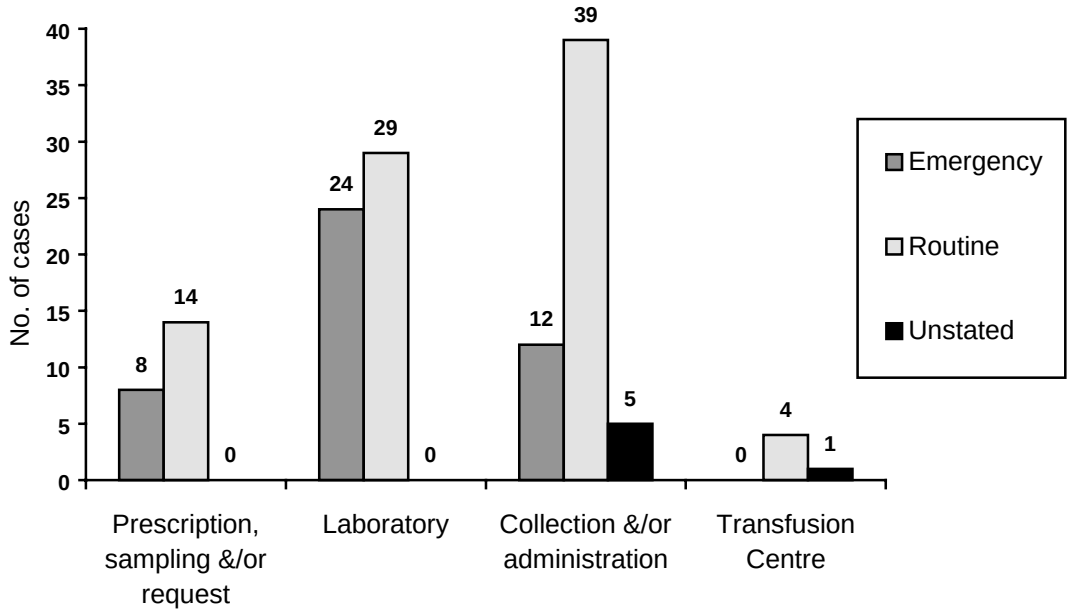
Analysis of reported errors

The questionnaire 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, in order to identify areas for improvement.

The data from 136 completed questionnaires are presented. 5 additional cases were considered but then excluded (see table 6) including one case where, in the presence of known multiple red cells antibodies, a deliberate clinical decision was taken to transfuse in an emergency with unselected red cells. There were no adverse sequelae and in the opinion of the authors this did not constitute a transfusion error, since such medical decisions may have to be taken in emergency situations.

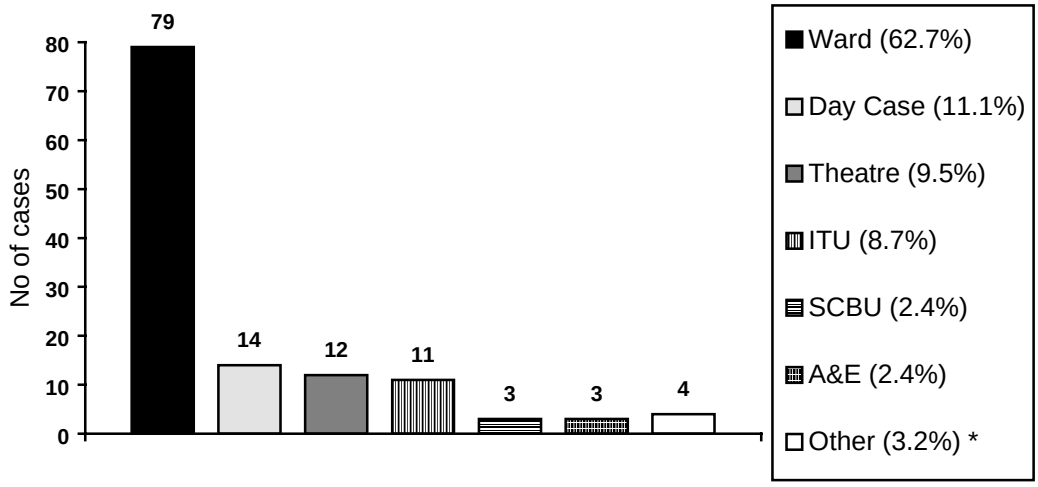
Of the 136 completed questionnaires, 86 related to routine and 44 to emergency transfusions. 6 questionnaires did not state whether routine or emergency. Figure 8 shows the distribution of errors relating to routine and emergency transfusions.

Figure 8
Incidence of errors at the various stages of the process of emergency and routine transfusion (n=136)



The questionnaire asked for information about where the transfusion took place. 126 reports gave information on the site of the transfusion. Unfortunately this information is of limited value as no denominator data are available. Figure 9 summarises this data

Figure 9
Site of transfusion

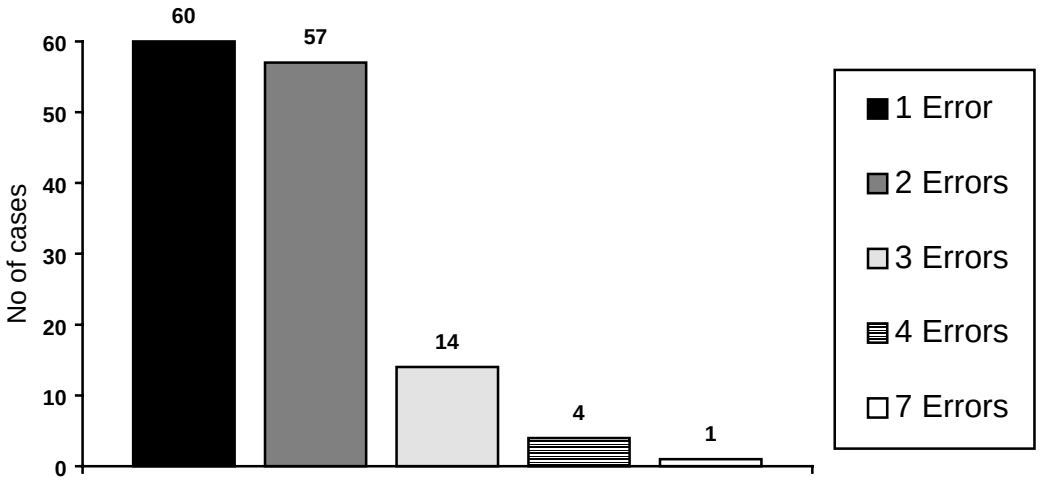


* 1 Acute Assessment Unit
2 Delivery Ward
1 Home address

Multiple errors contribute to many “wrong blood” episodes

Clinicians were asked to report the particular error which had been recognised as the cause of the incorrect transfusion. However, as in the previous two years, closer analysis of the questionnaires revealed that in 55% (75 cases) multiple errors had occurred in the transfusion process such that in 136 fully reported incidents a total of 239 procedural errors was identified. Figure 10 shows the number of errors per case

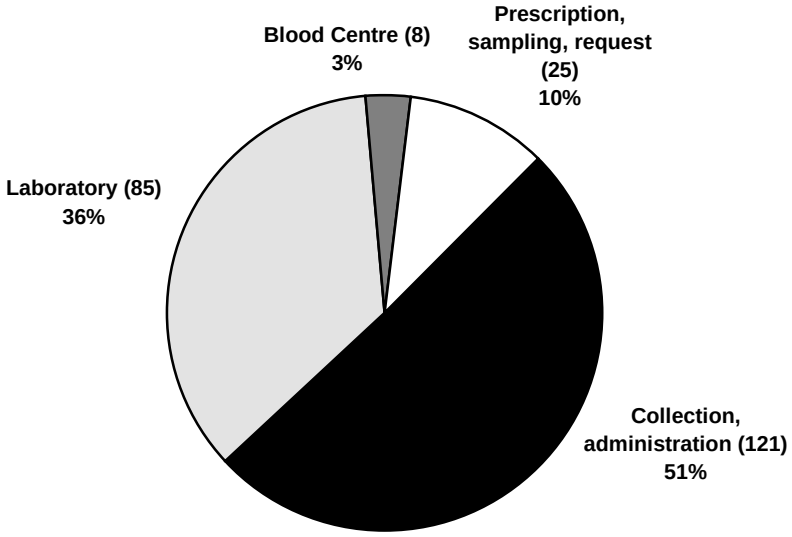
Figure 10
Total number of errors per case (total cases = 136; total errors = 239)



Distribution of errors

The following Pie chart shows the distribution, according to four main reporting categories, of a total of 239 errors from the analysis of 136 completed reports:

Figure 11
Distribution of total errors according to the main reporting categories (n=239)



A more detailed analysis of the distribution of total errors can be found in Table 8

Table 8
Distribution of procedural failures in terms of total errors. (n=239)

Location	Number of errors
Prescription, sampling and request	
Prescription of inappropriate and/or incompatible component	15
Details on request form incorrect	4
Details on sample incorrect	4
Sample taken from wrong patient	2
Total	**25**
Hospital blood bank	
Transposition of samples	5
Failure to consult/heed historical record	22
Incorrect group	15
Missed antibody on screening	2
Missed incompatibility	8
Selection /issue of inappropriate component	12
Incorrect labelling of component	7
Incorrect issue voucher	2
Clerical error	2
Failure to clear satellite refrigerator	3
Other procedural failure	7
Total	**85**
Collection and administration	
Collection of incorrect component	30
Failure of bedside checking process	60
Identification wristband missing/incorrect	16
Inappropriate component selected by clinician	5
Other procedural failure	10
Total	**121**
Supplying blood centre	
Incorrect group	1
Inappropriate component supplied	6
Incorrect serology results supplied	1
Total	**8**

The pitfalls of a complex multi-step, multi-disciplinary process

As has been pointed out in our first two reports, ensuring that the right patient receives the right transfusion at the right time is a complex multi-step process which crosses several professional and managerial boundaries and may involve many individuals. The following analysis of 239 procedural errors occurring in 136 completed reports reveals in more detail how events combined to result in "wrong blood" incidents.

Errors in prescription, requesting of blood components and patient sampling

There were 25 errors in this category occurring in 24 case reports.

Prescription errors

No cases of mis-prescribing were recorded this year although in 4 cases a decision was taken at the bedside to transfuse inappropriate components (see later).

Failure to request the appropriate component

In 15 cases there was failure to request the appropriate component. The most common error was failure to request irradiated components for patients at risk, notably 3 patients being treated with fludarabine, 2 neonates with a history of previous intra-uterine transfusion and 2 patients with Hodgkin's disease. In 3 cases there was failure to request CMV seronegative components (including one failure also to irradiate) for at risk patients; 2 of these were telephoned requests. No instances of TA-GVHD or CMV infection resulted from these errors. In one case there was failure to request Jka negative red cells for a patient with previous anti-Jka, not detectable at that time by laboratory tests. The patient suffered no adverse sequelae. It was not clear from the report whether the length of follow-up would have been sufficient to detect adverse sequelae. In another case a muddled telephone request contributed to the administration of cryoprecipitate in mistake for cryo-poor plasma.

Sampling errors

There were 2 cases involving the taking of samples from the wrong patient.

Case study 1: Failure to securely identify multiple "unknown patient " accident victims

Following a road traffic accident several severely injured casualties were admitted to an Accident and Emergency department. The hospital's policy for the secure identification of unknown patients was not followed resulting in a confusing combination of names and numbers. As a result a group A "unknown male" was transfused with 27 units of group O red cells. No adverse sequelae resulted from this although the patient remained severely ill as a result of his injuries.

Case study 2: Confusion over maternal and neonatal samples and the dangers of using pre-labelled sample tubes

A group O neonate received an emergency transfusion in theatre of group A red cells. The patient had no detectable anti-A and suffered no ill effects as a result of the major ABO incompatible transfusion. The error arose when a doctor at the referring hospital took blood samples which were tested in the hospital to which the baby was transferred for treatment. Samples were dispensed into pre-labelled tubes and maternal blood was placed in both sets of tubes, one of which was labelled for the baby.

Labelling errors

Errors in the labelling of request forms and/or samples were noted on 8 occasions. In all cases multiple errors in the transfusion process contributed to wrong transfusions but in only one case was the sample tube/ request form labelling error directly linked to the transfusion error. In the other 3 cases subsequent laboratory and/or bedside errors contributed to "wrong blood" incidents or other inappropriate transfusions.

Case study 3: Right blood, right patient, by good fortune

For a patient requiring a routine transfusion, incorrect identification details (mis-spelled surname) were supplied on the request form and sample tube. This error was carried through the laboratory documentation and subsequently to the ward. On noticing a discrepancy between details on the blood pack and patient identification details on the ward, the nurse assumed identity from the date of birth and hospital number.
Two other similar cases were noted. In other circumstances such lapses in protocol may have resulted in "wrong blood" transfusions.

Hospital blood bank errors

As in previous years, errors were not restricted to either inexperienced staff or to "out of hours" situations.
Of the 85 laboratory errors noted in 68 case reports, 41 occurred during routine working hours. 39 of these involved state registered MLSOs and 2 errors were made by a driver / health care assistant who had been authorised to collect blood products without reference to an MLSO. 43 errors involved staff working on-call of whom 19 were MLSOs working regularly in the laboratory and 24 were MLSOs who were not working regularly in the blood bank. In one case the grade of staff was not stated. This is summarised in Figure 12. Table 9 gives more detail about the errors and the grades of staff involved. Although 50% of laboratory errors occurred out of hours, in the absence of denominator data for the distribution of work it is not possible to comment on the significance of this finding.

Figure 12
Circumstances under which laboratory errors occurred (n=85)

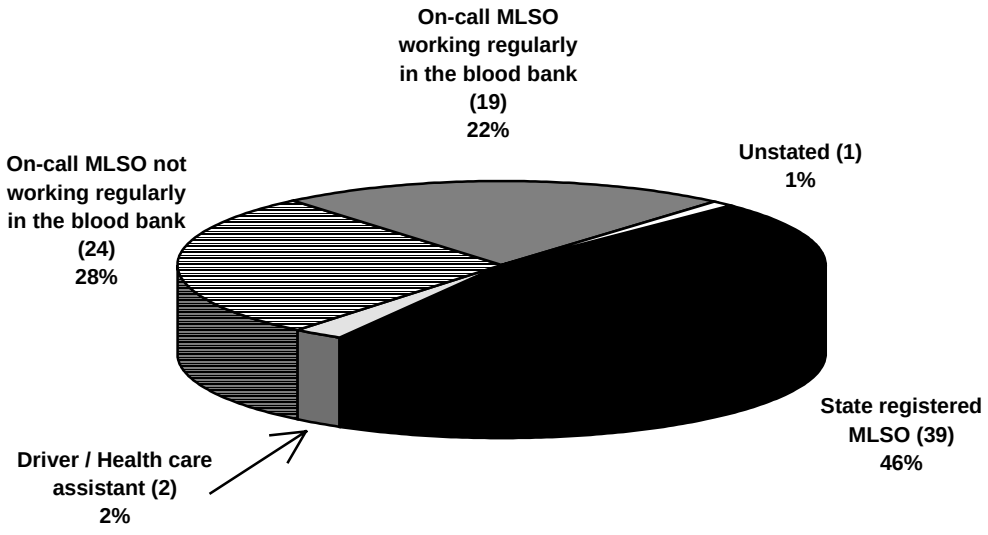


Table 9
Laboratory errors and grade of staff involved (n=68)

Error	Total number of errors	State registered MLSO, routine, regularly in blood bank	State registered MLSO, on call, regularly in blood bank	State registered MLSO, on call, not regularly in blood bank	Other Staff	Unstated
Transposition of samples	5	2	3	0	0	0
Failure to consult/heed historical record	22	10	4	7	1	0
Incorrect group	15	6	3	6	0	0
Missed antibody screen	2	2	0	0	0	0
Missed incompatibility	8	4	3	1	0	0
Incorrect labelling of component	7	3	1	2	0	1
Incorrect issue voucher	2	0	2	0	0	0
Inappropriate selection/issue	12	6	2	3	1	0
Failure to clear satellite store	3	3	0	0	0	0
Clerical error	2	0	1	1	0	0
Other procedural error	7	3	2	2	0	0
Total	85	39	21	22	2	1

Transposition of samples

5 errors fell into this category, 4 resulting in the transfusion of ABO incompatible red cells. 3 patients survived with no ill effects (one suffered an acute transfusion reaction) but one died, possibly related to the adverse effects of the transfusion.

Failure to consult/act on the historical blood bank record

There were 22 of these errors which ranged from failure to note special requirements for irradiation and/or CMV negative components to failure to detect ABO or RhD grouping discrepancies as illustrated in case 4 below. Such errors usually occurred in association with other errors either of request or other laboratory errors.

Case study 4: Failure to check the blood bank record removes a safety net

A 26 year old RhD negative female patient required emergency transfusion. The historical record was not consulted and RhD mis-typing resulted in the transfusion of two units of RhD positive red cells. She was treated with exchange transfusion and anti D immunoglobulin.

Grouping, screening and cross-match errors

25 errors occurred in these categories including 2 clerical errors. There were 13 errors of RhD typing (including the 2 clerical errors) resulting in the transfusion of RhD positive red cells to RhD negative

patients. 3 grouping errors resulted in the transfusion of ABO incompatible red cells, without adverse effects. 2 cases of RhD mis-typing resulted in the unnecessary administration of anti D immunoglobulin to patients who were, in fact, RhD positive. 2 further errors resulted in the transfusion of incompatible FFP, again with no adverse sequelae. Also in this group were 2 instances of missed positive antibody screens and 8 of missed incompatibility. In 2 cases antibody screen and cross-match failed to detect anti-Jka reacting only with homozygous cells. The remaining cases involved failure to detect other red cell antibodies which, in the opinion of the reporters, should have been detected.

Selection of an inappropriate component

This group (12 errors in total) comprised inappropriate selection of RhD positive red cells for a woman of child bearing potential (1 case), incorrect serological reasoning resulting in the issue of incompatible FFP, issue of outdated red cells, failure to irradiate and issue of the wrong component entirely (cryoprecipitate in place of cryo-poor plasma or paediatric FFP). In some cases the bedside check was deemed to have failed but in others it was not clear whether the bedside check would have been expected to detect the error, whilst in one case a deliberate clinical decision was taken to transfuse outdated red cells for a routine transfusion in theatre despite advice from the laboratory to the contrary. No adverse sequelae resulted from any of these incidents.

Case study 5: Incorrect serological reasoning by multiple health care personnel.

Eleven units of group O cryo-poor FFP were issued to a group A patient with thrombotic thrombocytopenic purpura being treated with plasma exchange. An unsupervised health care assistant overrode computer warnings and at the bedside, a nurse and doctor supervised the transfusion of the incompatible plasma. The patient suffered no adverse effects although the direct antiglobulin test became positive.

Incorrect labelling of component and/or issue voucher

9 errors of incorrect labelling of the component and/or issue voucher resulted in 3 ABO and 2 RhD incompatible transfusions. In 2 cases where the label pertaining to the intended unit was attached to a wrong unit, it was questionable whether the bedside checking procedure, if correctly carried out, would have detected the discrepancies.

Case study 6: Erroneous compatibility labelling which resulted in major ABO incompatibility
A group O woman undergoing Caesarean section was transfused with one unit of group B red cells bearing the correct (for the patient) group O compatibility label which had been applied in the hospital blood bank. Bedside checks failed to detect the discrepancy which would have been apparent if the compatibility label details had been compared with the original Blood Centre group label on the pack, which was correct. The patient recovered from the effects of intravascular haemolysis.

Problems relating to satellite storage sites

Failure to clear stocks of components from satellite storage sites resulted in the transfusion of out-dated or incompatible red cells. Whilst some errors were attributed to failures in the hospital blood bank, 3 other errors resulted from failure to heed a satellite refrigerator alarm and its subsequent deliberate deactivation by clinical staff (see 'Other procedural failures' later). These incidents serve to highlight the confusion which surrounds the management of satellite blood component storage areas in some hospitals.

Case study 7: Failure to "de-reserve" blood following an earlier transfusion leads to acute intravascular haemolysis

A patient with a negative red cell antibody screen had been transfused during a surgical procedure five days earlier. A further cross-match was requested for post-operative anaemia, at which stage the patient was found to have developed anti- Jka. Instead of using the newly cross-matched blood, a unit cross-matched five days earlier was taken from a satellite store which should have been cleared of the

"old" blood three days earlier. It was not clear from the report whether the responsibility for this task lay with the laboratory or clinical staff. The patient recovered from the effects of acute intravascular haemolysis.

Other procedural errors which resulted in the transfusion of an inappropriate component

This included computer warnings overridden or ignored, failure to check a blood centre delivery note against the inventory, resulting in the transfusion of an incorrectly stored component, and failure to inform senior laboratory staff of clinical use of an outdated component.

Errors in the collection and administration of blood components

121 errors fell into this category, occurring in 74 case reports.

Collection of incorrect component

30 incidents occurred in this category indicating that, as in previous years, the withdrawal of an incorrect component from its storage site continues to be a significant source of error. Errors were not restricted to specific groups or grades of staff and occurred whether or not formal checks were made at the time of collection. (Table 10)

Table 10
Collection errors according to grade of staff involved and whether or not a formal check was made at this stage (n=30).

GRADE OF STAFF	FORMAL ID CHECK		
	YES	NO	Unknown
Registered Nurse	7	8	0
Unregistered Nurse	1	2	0
Porter	1	5	1
Other		1	1
Unknown		1	2
TOTALS	**9**	**17**	**4**

Collection errors were always followed by failure of some aspect of the bedside checking procedure illustrating how mistakes at this important intermediate stage in the transfusion process set the scene for subsequent errors resulting in "wrong blood" incidents.

Failure of the bedside checking procedure

The 60 incidents which fell into this category comprised 25% of all procedural errors. Fifty cases resulted in "wrong blood" transfusions. In some cases bedside errors were preceded by laboratory or collection errors but the common factor was failure, in some way, of the final, vital bedside check which resulted in mis-identification of the patient. "Wrong blood" incidents resulted in 19 cases of major ABO incompatibility which included one case of earlier mis-labelling in the hospital laboratory. 24 ABO compatible and 6 RhD incompatible transfusions were given and there was one case of administration of anti D immunoglobulin to the wrong woman. Where mis-labelling had occurred in the laboratory, resulting in the application of the correct (for the intended patient) compatibility label to the wrong unit, bedside checks failed to identify the preceding error, as in case study 6 above.

Causes of mis-identification included remote checking of the component at the nurses' station rather than at the patient's bedside, confusion of patients with the same or similar names and failure to check the component label details against the patient. On more than one occasion component details were checked against the accompanying paperwork not with the patient's identity wristband. Failure to follow hospital policies for outpatient transfusions was also noted. Mistakes occurred even when two individuals rather than one were involved in the checking procedure, as can be seen in table 11.

Table 11
Grades of staff involved in bedside mis-identification incidents (n=60)

Grade of staff	Number of cases
Registered nurse & registered nurse	37
Registered nurse & doctor	5
Registered nurse & unknown	2
Registered nurse & unregistered nurse	1
Doctor & other	2
Doctor only	1
Registered nurse only	4
Other only	1

*excludes 7 cases where the grade of staff was not reported

Case study 8: Death from major ABO incompatibility in a patient for whom transfusion had not been prescribed

In this case confusion over two patients with the same surname resulted in the mis-transfusion of a group O patient who, although anaemic, had only been requested for a "group and screen", not cross-match. Following a check on only the surname on the compatibility label the wrong unit was collected from its storage site. Following subsequent failure of the bedside check over 100 ml of group A red cells were transfused. The patient complained of generalised pain and a transfusion reaction was queried but not acted upon. The patient became very ill and died within six hours of the transfusion. After the incident wording on compatibility labels was changed to include "not to be used for patient identification - always check blood against the patient's prescription chart and wristband".

Case study 9: Interruption of the checking process results in a major ABO incompatible transfusion

During a routine inpatient transfusion at night a group O patient received a few millilitres of group A red cells. The patient was not wearing a wristband. Prior to setting up the transfusion two registered nurses checked the blood in the ward treatment room in accordance with local policy. At the end of this process they were interrupted by the need to attend to a patient and in the meantime a further unit of blood for another patient was delivered to the treatment room. On returning the nurse picked up the unit she thought she had checked and connected it to the patient. Minutes later she realised that a final check had not been made and returned to the bedside to discover the wrong unit had been put up. The transfusion was immediately stopped and appropriate action taken. The patient suffered no ill effects. The hospital conducted a thorough review and made several recommendations including one recommendation to avoid routine transfusions at night.

Problems with identification wristbands

In 15 cases identification wristbands were missing and in one case the wristband contained the wrong information (incorrect hospital number). Analysis of the circumstances of missing wristbands revealed that 7 cases (47%) related to outpatient transfusions, 5 of which were mis-identification incidents. This should be considered in the context that 11.1% of transfusions in the IBCT category were given in the outpatient setting. Of these incidents, 2 resulted in major ABO incompatibility and 3 were ABO compatible. In the other cases (5 on the ward and one each in ICU, A+E and theatre) which involved mis-identification, 2 resulted in major ABO incompatibility, one RhD incompatibility and 4 were ABO compatible. In 3 other cases (failure to irradiate, transfusion of outdated blood) the missing wristband was an incidental finding.

Case studies 10 and 11: The dangers of outpatient transfusions

Case study 10: Two patients being transfused in an outpatient setting shared the same drip stand. The lines became entangled and a unit of red cells intended for one patient ended up being transfused to

the other patient. Fortunately the unit was ABO /Rh compatible. Hospital policy for checking of transfusions was not followed.
Case study 11: A patient requiring outpatient transfusion received the wrong ABO compatible unit. The circumstances leading up to this mis-transfusion included placing the case notes on an empty bed in anticipation of the patient's arrival and asking the patient to confirm identification details with a yes/no answer rather than requesting the patient to recite name and date of birth. Again, hospital policies were not followed.
In neither of theses cases was the patient wearing an identification wristband.

Inappropriate component selected by clinician

5 cases fell into this category and 4 involved confusion about the use of emergency un-crossmatched group O red cells. The fifth case involved the transfusion of incompatible FFP. All 5 occurred in the setting of emergency transfusions. The first 4 cases can be summarised as follows:

- The mistaken use of group O negative blood cross-matched for another patient because the emergency O negative blood could not be found
- The use of O positive red cells cross-matched for another patient in mistake for emergency O negative blood because both were stored in the same drawer of the refrigerator instead of in separate drawers.
- The use of "flying squad" O negative blood for an obstetric emergency patient with known anti c.
- The use of emergency O positive instead of O negative red cells for a group O negative obstetric emergency.

Incidents of incorrect serological reasoning resulting in the transfusion of incompatible plasma have been previously mentioned.

Other procedural failures

This comprised a miscellaneous group not easily classifiable elsewhere in this section and included the following incidents:

- Over-transfusion of a neonate at a rate of 50 ml hourly for four hours (i.e. a total of 200 ml given) instead of 50 ml over four hours.
- Drip put up on the wrong identical twin and subsequently the wrong twin transfused.
- Failure to act on and subsequent deactivation of a satellite refrigerator alarm (previously mentioned)
- Overruling of protocol with respect to incorrectly labelled blood packs (previously mentioned)

Errors originating at the supplying blood centre

Eight of these were reported this year and comprised the following:

- One grouping error: group $A_{weak}B$ typed as group B
- Two failures to supply appropriate component (irradiated, leucodepleted)
- One incorrect red cell serology result reported to hospital
- Four "out of specification" (with respect to storage conditions or date) components supplied

Outcome

Of 136 fully analysed reports there were 35 cases of major ABO incompatibility, including one case which was also RhD incompatible, 21 cases of Rh incompatibility (20 RhD and one Rh c) and 12 cases where other red cell incompatible transfusions were given. 28 "wrong blood" incidents were ABO/Rh compatible.

The remaining cases were inappropriate transfusions with respect to special requirements for irradiation, CMV negativity or leucodepletion (n=22), wrong component transfused (n=2), other breaches of protocol (n=11) and inappropriate administration of anti D immunoglobulin (n=5).

- One patient died as a result of major ABO incompatibility
- The deaths of two patients were possibly related to the transfusion
- Ten patients died from unrelated causes
- Five patients recovered from intravascular haemolysis
- Seven RhD negative females of child-bearing potential were exposed to RhD positive red cells
- 108 patients suffered no lasting ill effects although a few manifested acute transfusion reactions

Table 12 summarises the above outcome information.

Table 12
Outcome of cases of incorrect blood component transfused (n=136)

Category	Survived/ no ill effects	Major morbidity	Died/ unrelated	Died/ possibly related	Died/ definitely related	Unknown	Total
ABO/Rh incompatible	24	4[1]	3	2	1	1	35
Rh incompatible	13	7[2]	1				21
ABO/Rh [3] compatible	27		1				28
Other red cell incompatibility	8	1[1]	2			1	12
Inappropriate transfusion							
Special requirements not met[4]	22						22
Wrong component	1		1				2
Other[5]	8		2			1	11
Anti D immunoglobulin	5						5
Total	**108**	**12**	**10**	**2**	**1**	**3**	**136**

1 Recovered from intravascular haemolysis
2 Potential RhD sensitisation in females of child-bearing potential
3 Includes 3 cases of procedural failure but "right blood to right patient"
4 CMV negative/irradiation/leucodepleted
5 Out of date/ inappropriate storage/over-transfusion

Procedural Review

All reporters were asked to state whether the incident had been reported to their Hospital Transfusion Committees.

Table 13
Hospital Transfusion Committees

Number of Responses	Response

9	No response
79	Not yet, but will be discussed at a future meeting
17	No Transfusion Committee exists at time of reporting
26	Yes
***131**	

* There were an additional 5 incidents for which no procedural review data was available:
1 incident involved a Blood Centre error which was reported by the centre itself
4 incidents were reported by letter rather than questionnaire

Reporters were also asked whether any changes had been made to policies / procedures as a result of the incident. 78 replied that changes had been made and 3 said that that the issue was "under discussion" at the time of reporting. 14 reporters stated that the error(s) resulted from a failure to follow existing adequate procedures. In these cases 11 recommended reiteration of current policy to all staff involved and 3 said that the individual members of staff concerned had been counselled or disciplined. In one incident the error was discovered some considerable time after the event and the source of the error could not then be identified. 34 reporters did not respond at all to the question of procedural change.

Recommended changes

Of the 78 respondents who stated that changes had been made the replies fell into the following categories:

- Changes implemented to documentation; collecting; handling; laboratory techniques/procedures; ward procedures/protocols; administration (n = 45)
- Implementation of new / additional training (n = 11)
- Review of existing policies / procedures / protocols (n = 18)
- Review of training requirements (n = 2)
- Recommendation to appoint new / additional staff (n = 1)
- Upgrade or renewal of equipment (n = 3)
- Dissemination of information (n = 6)
- Consideration given to introduction of innovative techniques / procedures (n = 7)

Overall there is evidence that hospitals are striving hard to improve the quality of transfusion practice and that serious incidents are investigated promptly and thoroughly with appropriate action being taken to guard against a recurrence.

COMMENTARY

- For the third year running the most important single cause contributing to mis-transfusion was failure of some aspect of the bedside checking procedure immediately prior to administering the transfusion. Causes included remote checking at the nurses' station or treatment room rather than at the bedside, checking the component against the accompanying paperwork not the patient and failure to note discrepancies between compatibility and donation labels where preceding laboratory labelling errors had occurred. There was some evidence to suggest that interruption during this critical step may have played a significant part in failure of the process.

- The absence of patient identification wristbands or alternative formal means of identification was noted on 15 occasions, 47% of which were related to outpatient transfusions. These omissions contributed to "wrong blood" incidents.

- The withdrawal of the wrong pack from its storage location in the hospital continues to be a common error and in this report was always followed by mis-identification at the bedside.

- The historical transfusion record was not checked or there was failure to act on relevant information in 22 instances. Such errors usually occurred in association with errors in other parts of the transfusion chain.

- Laboratory incidents included 25 errors of grouping, antibody screening and cross-matching, 5 cases where samples were transposed and 9 labelling errors. 50% of laboratory errors occurred "out of hours" but there is insufficient data to ascertain the significance of this finding.

- There were 15 cases of failure to request the appropriate component, most commonly irradiated components for patients being treated with purine analogues (fludarabine), neonates with a history of intra-uterine transfusion and patients with Hodgkin's disease. Failure at this point was often combined with inadequacies in the hospital blood bank record system.

- There were several incidents of the selection, issue and transfusion of incompatible plasma, as a result of incorrect serological reasoning, and 2 cases where cryoprecipitate was transfused in mistake for cryo-poor FFP in one case and paediatric FFP in the other case.

- Several problems arose in relation to the management of satellite storage refrigerators. These included failure to clear stocks of blood previously cross-matched for individual patients, failure to act on and subsequent deliberate deactivation of an alarm and confusion over the storage and use of emergency stocks of group O red cells. Each incident lead to the administration of inappropriate components and included one case of intravascular haemolysis.

- Confusion over telephone messages appeared to be a factor in some errors.

- Although there were only 2 cases of samples being taken from the wrong patient these errors were solely responsible for wrong blood transfusions and occurred in "classic" settings: confusion between two unknown accident victims and a mix-up over maternal and infant samples. In the latter case pre-labelled tubes were used.

RECOMMENDATIONS

"Wrong blood" incidents are without exception avoidable errors and it cannot be over-emphasised that the bedside check is the final, vital step in preventing mis-transfusion.

- **Every hospital must have a formal policy for the bedside check which must be rigidly enforced on all occasions.**

The procedure must ensure that components can be allocated to the correct patient and that previous laboratory labelling errors can be detected. Hospitals must ensure that staff undertaking this important task receive correct training.

- **The environment in which the transfusion is conducted must provide adequate working space, and allow staff responsible for the bedside check to carry out an uninterrupted checking procedure.**

Further investigation of the timing of transfusion errors may identify weak areas in the transfusion process, particularly out of hours, and enable steps to be taken to minimise the number of "out-of hours" transfusions.

- **Hospital systems must ensure that there are no exceptions with regard to the provision of patient identity wristbands or their equivalent**.

This is particularly important in the outpatient setting where familiarity with the patient may lead to a tendency to cut corners in the formal checking procedure.

- **Computerised identification systems are available to ensure safe transfusion at the bedside. These systems must now be evaluated.**

- **Hospitals must ensure that standards are set for minimum formal identification requirements and that staff responsible for this stage are aware of the key role which they play and are properly trained in the procedure.**

The correct collection of blood components from the hospital storage location is an essential intermediate step in the transfusion process. Mistakes at this point set the scene for subsequent errors resulting in wrong blood incidents.

- **The historical transfusion record must be available, consulted and acted upon at all times.**

It is an essential tool in ensuring the safety of the transfusion process. Access to information about previous grouping and special requirements may prevent a mis-transfusion.

- **Blood banks must continue to be vigilant in reviewing procedures, systems and training to prevent sample handling and technical errors**.

Despite increasing automation and computerisation in hospital laboratories transfusion testing remains an area where skill as well as training to established procedures are of paramount importance.

- **Individuals responsible for the prescription and request of blood components must be familiar with the special requirements of their patients. These requirements must be flagged on the patient's clinical and laboratory records.**

- **Staff prescribing and/or handling blood components must be educated with respect to their recognition and correct use.**

- **Hospitals must develop unambiguous protocols for the management of satellite refrigerators and their stocks**.

- **Telephoned requests for blood components must be formally recorded and incorporate all relevant information including special requirements.**
- **Staff responsible for taking samples for transfusion testing must at all times follow strict procedures to avoid confusion between patients at the time of sampling. Sample tubes must never be pre-labelled and labelling must be completed for one patient before moving on to the next. Special care is required when dealing with "unknown" multiple casualties**

- ***Advice on many of the above areas can be found in the recently published BCSH guideline "The administration of blood and blood components and the management of transfused patients"[5]. This guideline has been reproduced in Appendix 8.***

8. ACUTE TRANSFUSION REACTIONS

Definition
Acute transfusion reactions were 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 7

This category accounted for 13.9% of non-infectious hazards reported.

Forty three initial reports (40 new) were received, but of these, 4 were not, in fact, thought to be reactions to blood components (1 to desferrioxamine, 1 to intravenous immunoglobulin, 1 to prostaglandin E2 and 1 not stated). After careful consideration a further 3 were withdrawn (including 1 from last year) because insufficient information could be obtained. 34 completed questionnaires were received. These included 2 cases for which initial notification forms were received in the previous reporting year. 2 reports are outstanding and will be analysed next year.

This chapter highlights the main findings from 34 completed questionnaires.

Overall there were 3 deaths in this group, 1 following red cells, 1 following FFP and 1 in a patient who received both FFP and platelets. In two cases the deaths were thought possibly related to the transfusion reaction (one patient with acute liver failure who developed angio-oedema and one patient with a massive gastro-intestinal bleed who developed dyspnoea) while in the third the death was unrelated to the transfusion (gastrointestinal haemorrhage). In all three cases the patients were severely ill and the deaths seemed primarily related to their underlying disease. One patient required admission to ITU following an anaphylactic reaction to FFP but subsequently made a good recovery. All the remaining patients suffered minor, or no, morbidity.

Sex (42 reports)

Males	24
Females	18

Age (38 reports)

Age range	17 months - 92 years
Median	56 years

Components implicated (34 reports)

Red Cells (RBC)	17 (1 including concomitant FFP)
Fresh frozen plasma (FFP)	10
Platelets	7 (1 including concomitant FFP)

1. Reactions in which red cells were implicated

There were 17 cases (including 1 case receiving red cells and FFP) and all but 1 survived without long term sequelae. The following reactions were seen:

Reaction type	Number of cases
Non-haemolytic febrile	8
Anaphylactic[1]	3
Allergic[2]	3
Dyspnoea/chest pain/rigors	1
Jaundice	1
Haemoglobinuria	1

[1]anaphylactic/anaphylactoid (defined as: hypotension with one or more of: rash, dyspnoea, angioedema)
[2]allergic (defined as: one or more of the following - rash, dyspnoea or angioedema **without** hypotension)

Non-haemolytic febrile transfusion reactions (NHFTR)

Most NHFTRs are not regarded as serious sequelae and therefore SHOT does not set out to collect reports of these types of reactions. Nevertheless, 8 reports fell into this category and in all cases the reaction started while the transfusion was in progress.
In one case a mixed growth of *Staphylococcus epidermidis* was obtained from the pack but the patient had no blood cultures drawn (and received no antibiotics) and so it is assumed that this was not a bacterial reaction and that the *Staph* was a laboratory contaminant. In one case HLA antibodies were demonstrated. No diagnostic investigations were carried out in the remaining patients.
In 2 cases a pre-existing red cell antibody was missed in the pre-transfusion testing (see below). It is not known what role, if any, the antibody may have had in the transfusion reaction.

- *a 76 year old female with multiple myeloma, admitted with a fractured neck of femur suffered fever and rigors during transfusion of 1 unit of red cells. The blood had been issued after grouping by tile technique and no antibody screen had been performed (the hospital's "routine" out-of-hours practice). A LISS-IAT cross-match in tube did not detect any incompatibility. Retrospective antibody screen revealed the presence of anti-K in the pre-transfusion sample but the K status of the unit is not known.*

- *a 42 year old female with gastrointestinal bleeding developed fever and rigors after the transfusion of 50ml of red cells. A pre-transfusion antibody screen and identification panel (10 cells) showed the presence of anti-E. However, a second sample, drawn only 30 minutes later showed both anti-E and anti-s. There was no laboratory evidence of haemolysis.*

Anaphylactic/anaphylactoid reactions

Three patients developed hypotension in association with fever or rigors and a rash or dyspnoea.

- *a 16 year old boy undergoing spinal surgery developed hypotension, fever, rash and respiratory problems after receiving only around 5-10ml of red cells. He had a history of previous transfusion. He responded to adrenaline and steroids and was subsequently shown to have IgA deficiency with IgA antibodies. Subsequent transfusion with washed red cells was tolerated without incident.*

- *An 18 year old male receiving a transfusion of laboratory-leucodepleted red cells for thalassaemia developed hypotension, rash and fever. He responded to IV colloid and crystalloid with steroids and an antihistamine. The patient had increased the speed of his red cell transfusion in order to attend a social event. No other cause was identified.*

- *a 42 year old woman with a post-partum bleed developed hypotension, rigors and dyspnoea after receiving 100ml of red cells through a bedside filter. She responded to antihistamines, steroids and oxygen. Although TRALI was suspected, investigation of donor and recipient revealed no white cell antibodies. The patient was known to be allergic to penicillin but the donor unit was not tested for the presence of this drug.*

Allergic reactions

There were three allergic reactions in this group, characterised by a rash or angioedema without hypotension. Two of these appertained to one patient:

- *a 45 year old woman being transfused because of a haematological malignancy developed rash, rigors and chest pain during transfusion of buffy-coat depleted red cells. She was subsequently shown to have IgA deficiency but with no detectable anti-IgA. Subsequent transfusions were of washed red cells but she reacted again about six weeks later. It was felt that the red cells had been inadequately washed on that occasion.*

- *a 16 month old girl being treated for acute myeloid leukaemia (AML) developed facial oedema during a laboratory-leucodepleted red cell transfusion. She had developed a similar reaction to leucocyte-depleted platelets a few weeks previously.*

Other reactions

- *a 92 year old woman became jaundiced a few hours after a post-operative transfusion. There was no evidence of acute haemolysis and no other cause was found. The role of the transfusion in this event was not clear.*

- *an 89 year old woman developed dyspnoea, chills, rigors and hypertension with peripheral cyanosis after receiving 100ml of non-leucodepleted red cells. Donor and patient were tested for granulocyte and HLA antibodies but this was negative. The patient subsequently died but this was not thought to be related to the transfusion reaction.*

- *an 82 year old female developed isolated haemoglobinuria during the transfusion of two units of red cells. No cause was identified and the Hb rose by 40g/l as a result of the two unit transfusion.*

2. Reactions in which fresh frozen plasma (FFP) was implicated

There were 10 reports in this group. Two patients, who were very ill due to bleeding varices or gastrointestinal bleeding at the time of component administration, died and the reaction may have contributed to their deaths. The remaining 8 patients survived without sequelae. Reactions occurred during (8 cases) or within 2 hours of stopping the transfusion (2 cases) and were of 2 main types:

Reaction type	Number of cases
Anaphylactic	6
Allergic	4

Anaphylactic/anaphylactoid reactions

There were 6 patients in this category and their reactions were characterised by hypotension with respiratory complications in 5. Two of these also had rash/pruritis with angioedema and anti-Gm1,3 was detected in one of these cases. The final patient, who was receiving angiotensin-converting enzyme (ACE) inhibitors had hypotension with bradycardia/systemic collapse and it is not clear if this was an anaphylactic response or somehow related to his medication. It should be noted that there is no clear distinction between transfusion-related acute lung injury and anaphylaxis in the absence of a rash or angioedema unless appropriate investigations (performed only in one of these cases) show the presence of potentially implicated antibodies.

Four patients were treated with steroids and a antihistamine, one received only a diuretic and one received steroids and adrenaline.

Allergic reactions (not anaphylaxis)

Four patients suffered apparent allergic reactions with dyspnoea and rash/pruritis. In three cases steroids and an antihistamine were given and two patients received adrenaline.

In the majority of cases investigations to identify the cause of the reactions had not been carried out.

3. Reactions in which platelets were implicated

There were 7 cases in this group (including 1 case in which FFP was also administered), 5 of which occurred during the transfusion and two within 2 hours after completion of infusion. All patients survived without ill effects.

Reaction type	Number of cases
Haemolytic	1
Anaphylactic	3
Allergic	2
Hypotension	1

- *A 36 year old woman, group A RhD positive received an apheresis unit of group O platelets for a post-partum haemorrhage. She developed evidence of intravascular haemolysis and a positive DAT within 2 hours of completing the transfusion. The donor had been tested to exclude high titre haemolysins (saline, 37^{o}C) but retrospective testing by IAT methods for IgG anti-A showed a titre of 1 in 20,000.*

- *Three patients experienced anaphylaxis, 2 with rash, dyspnoea and hypotension and one with rash and hypotension. In one case a bedside filter was in use. Only one patient was tested for IgA antibodies (negative) and although Gm3 antibodies were found in this patient, the platelet donation was Gm3 negative. One patient had multiple HLA antibodies.*

- *Two patients experienced allergic reactions with rash and dyspnoea. One of these, a 16 year old boy being treated for acute lymphoblastic leukaemia and who was receiving platelets through a bedside filter, also developed angioedema. In one case it was suggested that the patient's penicillin allergy may have been the cause although no donor or pack testing for this drug was carried out.*

- *A 64 year old female being treated for acute myeloblastic leukaemia developed hypotension and syncope within 15 minutes of completing a transfusion of a pool of laboratory-leucodepleted platelets. She was not on ACE inhibitors and there was no evidence of infection.*

Response times

In general patients were seen within minutes of the reaction developing and the local haematologist was contacted for advice in 21 cases (60%).

Observations

There was a wide range of frequency of nursing observations prior to the onset of the reaction:

Table 14
Frequency of nursing observations

Frequency of observations	Number of cases

5 minutes	2
10 minutes	3
15 minutes	6
30 minutes	6
60 minutes	2
Continuously monitored	6
Nil	2
No information	7
Total reporting	**34**

Reporting to Blood Centres and Hospital Transfusion Committees

This was highly variable, reflecting, perhaps, the wide range of reactions reported.

Table 15
Reporting of reactions to the local Blood Centre (BC) and the Hospital Transfusion Committees (HTC)

Reported to	Number
HTC only	2
BC only	10
HTC and BC	17
Neither	5
Total	**34**

COMMENTARY

- In two cases of acute reactions to red cells a pre-existing antibody was not identified, in the first instance because no antibody screen was carried out on a non-urgent, out-of-hours sample and in the second case a second antibody appears to have been missed (detected in a sample drawn 30 minutes later). In the first case the procedures for handling out-of-hours samples have been reviewed and altered.

- It is not the intention of SHOT to seek reports of non-haemolytic febrile transfusion reactions but 8 such reports were received. It is notable that some acute reactions due to undetected red cell antibodies are indistinguishable from febrile, non-haemolytic transfusion reactions if the patient has received only a small volume of blood. Clinicians should therefore be encouraged to report all reactions which they regard as serious.

- The reported use of laboratory leucocyte-depleted components was low (3 units of red cells, 3 units of platelets) and there was no clear association between laboratory leucodepletion or the use of bedside filters and the nature of the adverse event. Nevertheless, continued vigilance is recommended in order to detect any unexpected adverse reactions to this new technology.

- Two adverse events followed the administration of FFP to reduce the INR in warfarinised patients who were not bleeding. The BCSH Guidelines on Oral Anticoagulation[7] recommend that patients who have been anticoagulated with warfarin and who require reversal of anticoagulation should be managed by omitting the drug, administering vitamin K or, in cases of life-threatening haemorrhage by giving prothrombin complex concentrate(PCC). FFP is indicated only if PCC is unavailable and life-threatening bleeding is occurring[8].

- One platelet reaction seemed to be related to a high titre anti-A which was not detected by standard screening methods for high-titre agglutinins/haemolysins. It is recognised that the use of IAT methods for isoagglutinin detection will yield a result which may be five-fold higher than that obtained by direct techniques.

- Reactions, other than haemolytic reactions, to all components were, in general, not investigated to determine the cause of the reaction. However, in one case which was likely to be due to anti-IgA a second event followed inadequate washing of red cells, emphasising that some of these patients are extremely sensitive to very small residual amounts of plasma.

RECOMMENDATIONS

- Clinicians should continue to report all serious adverse events even if these are not currently recognised as "classical" acute transfusion reactions as this may act as an early alert to unusual adverse effects of novel techniques and processes (e.g. laboratory leucodepletion, virus inactivation, drug/product interactions).

- Reactions to platelets and FFP may be similar to TRALI but this diagnosis cannot be confirmed without appropriate investigations for donor and recipient white cell antibodies. It is recommended that such investigations are performed whenever respiratory symptoms are prominent.

- Administration of FFP and platelets should conform to published guidelines[8,9]. The use of FFP to reverse warfarin effect is rarely justified.

- If group O plasma (or platelets in plasma) is to be used for non-O recipients then those administering the unit should ensure that it does not contain high-titre ABO antibodies.

- Transfusion Services should re-examine their current screening methods for detection of potentially haemolytic titres of isohaemagglutinins to assess whether or not more sensitive methodology might be indicated in order to minimise the risk of haemolysis of recipient red cells.

- There remains a need for guidelines on the appropriate investigation of acute transfusion reactions and the British Committee for Standards in Haematology should consider this as a suitable topic for development of national guidelines.

9. 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 almost invariably delayed haemolytic reactions due to the development of red cell alloantibodies

This category accounted for 12.7% of non-infectious hazards reported.

34 initial reports were received (32 new) and 30 completed questionnaires were returned. One patient has been excluded as he had no transfusion reaction or detectable antibodies but was reported to SHOT because a historical record of Jka antibody was not taken into account when blood was selected for transfusion. In retrospect this case would, in fact, fall into the IBCT category but has not been included on this occasion. One case which had been carried forward from the previous year was withdrawn because insufficient information could be obtained. 2 questionnaires are outstanding and will be analysed next year. This chapter highlights the main findings from 30 completed questionnaires.

Sex

Males 7
Females 26

Age

Age range 21 - 90 years
Median age 67 years

Timing of Reaction/Diagnosis in relation to previous transfusion

Days post-transfusion	No. of cases
1-5	5
6-10	11
11-15	7
16-20	1
>20	4
Not stated	2

Range 1-75 days
Median 11 days

Reactions Reported

There were 3 deaths in this group of which one was related to the transfusion (Case 19) and 2 were due to the underlying disease. In addition, one patient required renal dialysis but subsequently made a good recovery. The remaining patients suffered minor, or no morbidity.

All reactions were related to the administration of allogeneic red cells but in 3 patients who seemed to have clear-cut haemolytic reactions no antibodies were detected or known from historical transfusion records. In total 34 new antibodies were noted in the 30 patients who suffered a delayed haemolytic transfusion reaction (DHTR), which for the purpose of this report is defined as evidence of haemolysis occurring more than 24 hours post-transfusion, whether or not a new red cell antibody has been identified. Strictly speaking 7 of these reactions were sensitisation episodes only - there was no evidence of haemolysis although 5 cases had a positive DAT. One case was reported because of detection of anti-K 75 days post-transfusion. These cases should probably be regarded as serological reactions, rather than delayed haemolytic transfusion reactions.

Seven patients had pre-transfusion red cell allo-antibodies. In one of these the antibody was not correctly identified and therefore appropriate blood was not selected. In the others, appropriately phenotyped units were selected.

One further patient (Case 24) had a historical record of anti-Jkb which was not communicated to second hospital to which the patient had been transferred. It was not detectable pre-transfusion but was detected 11 days post-transfusion.

Two reports were on 21 year old identical twin sisters with sickle cell disease. One was admitted for red cell exchange because of recent cerebral infarction. The other was admitted one month later with abdominal pain which may have required surgery and so a transfusion was given. In each case the patient developed severe anaemia 1-2 weeks later, reported as "suggestive of hyperhaemolysis syndrome". Serological investigations were negative. It is not known if these patients manifested an appropriate reticulocyte response or whether or not infection-related erythroblastopenia may have played a role. Both patients recovered without sequelae.

Urgency of Transfusion Requirement

In 22 patients the transfusion was said to be routine and in 7 urgent (one not stated). One patient was transfused for recurrent iron deficiency anaemia.

New Post-transfusion Antibodies

Table 16 shows the new post-transfusion antibodies according to antigen specificity and Table 17 gives details of these antibodies for individual patients.

Table 16
New post-transfusion red cell antibodies in 30 patients: according to antigen specificity

Antibody group	Number	Sole antibody
Kidd		
Jka	13[1,2]	7
Jkb	2	1
Duffy		
Fya	2	1
Kell		
K	3	3
Kpb	1[3]	1[3]
Rh		
Cw	1	
c	2	
E	8[4]	3[4]
Lutheran		
Lua	1	
Other		
Yka	1	1

[1] Previously known but not disclosed (1)
[2] Misidentified pre-transfusion (1)
[3] Autoanti-Kpb
[4] enzyme-only antibody pre-transfusion, IAT reactive one week post-transfusion (1)

Table 17
New post-transfusion red cell antibodies in individual patients

ID	Antibody(ies)	Comment
1	K	Pre-transfusion Fya and +ve DAT
2	E + Jka	Pre-transfusion E
3	Fya + Jka	
4	Jka	
5	K	
6	Jka	
7	Jka	
8	E + Cw	
9	Lua	Pre-transfusion E + Kpa + Auto. However, Lua unlikely to have caused fall in Hb
10	Jka	Pre-transfusion K
11	Jka	
12	c + E + Jka	
13	E	Pre-transfusion c, Cw, Fya
14	Jkb	
15	None	DHTR but no antibodies detected
16	Jka	
17	K	
18	E	
19	E	Enzyme-only E pre-transfusion and 4 days post. IAT reactive 7 days post. Died due to renal failure.
20	Jka	
21	E	
22	Jka	Present but mis-interpreted pre-transfusion
23	Yka	Developed auto-immune haemolysis post-transfusion
24	None	Pre-transfusion C + E + DAT +ve. Jkb known historically but not communicated. Not detectable pre-transfusion
25	Jka	
26	Auto-Kpb	Developed auto-immune haemolysis ?"triggered" by transfusion
27	None	?Hyperhaemolysis syndrome/?red cell aplasia in sickle, no antibodies
28	None	?Hyperhaemolysis syndrome/?red cell aplasia (twin of 27), no antibodies
29	Fya	Neg. at 4 days post, positive 11 days post
30	E, c, Jkb	

Clinical sequelae

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

- Group 1 Asymptomatic (± positive direct antiglobulin test (DAT) ± spherocytes)
- 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 6 patients in this group (cases 4, 5, 10, 11, 17, 21). All survived without sequelae.

Group 2
There were 10 patients in this group (cases 1, 2, 8, 14, 16, 25, 26, 27, 28, 30) of whom 9 survived without sequelae and 1 had to have planned surgery delayed due to the reaction.

Group 3
There were 11 patients in this group (cases 3, 6, 7, 12, 13, 15, 18, 22, 23, 24, 29) of whom 6 survived without sequelae, 2 died from unrelated causes, 1 experienced slowing of recovery from previous renal failure and 2 experienced ongoing fatigue and jaundice. In addition, one patient (case 29), who was already recovering from renal failure at the time of her reaction, was felt to have acquired more prolonged renal support than anticipated as a result of the transfusion reaction, but subsequently made a good recovery.

Group 4
There were 3 patients in this group (cases 9, 19, 20) of whom 1 died due to the transfusion reaction (case 19), 1 required readmission to hospital because of failure to cope secondary to her anaemia and the third survived without sequelae.

The above results are detailed in Table 18

Table 18
Grouping of cases by clinical sequelae of DHTR

Group 1		Group 2		Group 3		Group 4	
ID	**Antibody**	**ID**	**Antibody**	**ID**	**Antibody**	**ID**	**Antibody**
4	Jka	1	K	3	Fya + Jka	9	Lua + AIHA
5	K	2	E + Jka	6	Jka	19	E (enzyme)
10	Jka	8	E + Cw	7	Jka	20	Jka
11	Jka	14	Jkb	12	c + E + Jka		
17	K	16	Jka	13	E		
21	E	25	Jka	15	None		
		26	AIHA (Kpb)	18	E		
		27	None	22	Jka		
		28	None	23	Yka + AIHA		
		30	E, c, Jkb	24	Jkb		
				29	Fya		

Analysis of serological information

Antibody screening

Table 19 gives information on the serological methods used for antibody screening in the 30 reported cases.

Table 19
Summary of serological methods used for antibody screening

Screening Method	2 cell screen	3 cell screen	4 cell screen	Total
Tube LISS IAT	1	3		4
Column IAT	7	14		21
Solid Phase	1		2	3
Not done				1
Not known				1
Total	**9**	**17**	**2**	**30**

This table shows a preponderance of column technology for antibody screening in these cases. However, this is in keeping with NEQAS (Blood Transfusion Laboratory Practice) data which showed that 75.3% of NEQAS participants were using column technology for antibody screening in July 1998. Detailed assessment of the techniques used (serum:cell ratios, incubation times etc) was not carried out. In two instances a "rapid" rather than "routine" technique was employed. In 18 cases the pre-

transfusion sample was re-investigated and yielded the same results other than in one case in which an anti-Jka, present pre-transfusion, had not been appropriately identified.

At least 9 different suppliers of antibody screening cells were reported. There was no association between the cell supplier and apparent or possible non-detection of pre-existing antibodies.

Details of some unusual serological cases are given below:

- *Case 9 This 90 year old female received a transfusion for the anaemia of chronic disease. She had had many previous transfusions. Pre-transfusion she was noted to have anti-E, Kpa and autoantibodies reacting by LISS IAT and manual polybrene. The DAT was positive (IgG). Four days post-transfusion she developed jaundice with a falling Hb and renal impairment. Anti-Lua was noted in the post-transfusion sample in addition to the previously identified antibodies. It was felt unlikely that the anti-Lua had caused the degree of anaemia noted and this patient has probably experienced an exacerbation of auto-immune haemolytic anaemia.*

- *Case 19 A 68 year old female with multiple myeloma and a history of transfusion one month previously developed jaundice, falling Hb, haemoglobinuria and anuria 1-2 days following transfusion of two units of red cells. A pre-transfusion sample and a 4 day post-transfusion sample, screened by LISS IAT tube techniques and a 2 cell panel showed no antibody. However, testing of both samples by papain technique showed the presence of an anti-E in both samples. Repeat testing at 7 days post-transfusion showed that the antibody was now IAT reactive. Both transfused units were R2r. The patient developed renal failure and died as a result of this reaction. Death from the underlying myeloma was NOT expected at this point in the patient's care.*

- *Case 23 This 65 year old female was transfused for haemorrhage from a wound haematoma. Pre-transfusion testing showed no auto- or alloantibodies. Ten days post-transfusion she developed cramps, a raised bilirubin, falling Hb and a positive DAT (IgG). Investigation of post-transfusion sample showed the presence of anti-Yka and an autoantibody. Anti-Yka is not generally thought to be clinically significant. It was proposed that the transfusion may have stimulated an autoimmune haemolytic anaemia.*

In five cases the transfusion reaction occurred within 5 days of transfusion. This is perhaps the most interesting group in terms of possible “missed” antibodies. Three of this group had 2 or 3 antibodies detected in the pre-transfusion sample and each of these patients developed evident jaundice within 5 days of transfusion. In each case the presence of 2-3 antibodies was identified using only a single panel of cells. Two labs used both IAT and papain techniques while one used an IAT technique only.

- *Case 24 A 33 year old previously transfused male with AIDS and a lymphoma was identified as O RhD positive with anti-C + E. This would be an unusual combination in a Rh positive patient. These two antibodies were identified using a single 10 cell panel and a single column technology. He developed jaundice and falling Hb 3 days post-transfusion. Post-transfusion investigation revealed only anti- C + E but it was noted that anti-Jkb had been previously detected at the hospital which transferred the patient. The post-transfusion antibody identification was again performed using a single panel of cells and a single technique.*

- *Case 13 A 42 year old female with post-surgical bleeding had the presence of anti-c, Fya and Cw noted in the early 1980s. On this occasion these antibodies were “confirmed” using a single 11-cell panel by IAT and papain column agglutination techniques. The patient developed jaundice and anaemia 2-3 days post-transfusion and the post-transfusion sample was referred to the local transfusion centre where the presence of an additional anti-E was noted. This is unusual in that it would be expected that a patient with anti-c would have received R_1R_1 units (this detail was not clarified by the questionnaire). It is therefore not clear how the anti-E had arisen unless an R_1R_Z unit was administered.*

Cross-matching

Interval between drawing cross-match sample and transfusion

The interval between cross-matching and sampling is shown below for 30 reports

Interval between cross-matching and sampling (hrs)	No. of cases
0-47	23
48-71	2
72-96	2
>96	0
Not known	3

Cross-matching methods used

The methods used for cross-matching are shown below:

Method	No. of cases
Electronic cross-match	2
Immediate spin	3
LISS IAT Tube	8
Column	16
Not known	1
Total	**30**

In general, the timing of pre-transfusion samples was in keeping with the national guidelines[4]. It was not always possible to ascertain from the questionnaire the timing of an earlier transfusion and the implicated transfusion.

Reporting to Blood Centres and Hospital Transfusion Committees

Only 16/30(52%) of cases were reported to the local Blood Centre and 19/30 (62%) were reported to the Hospital Transfusion Committee. It is presumed that reporting hospitals felt that the local Blood Centre had nothing additional to contribute to the case and that there were no implications for recipients of other components from the same donor.

COMMENTARY

- In general there is little evidence of poor laboratory practice with the majority of DHTRs apparently occurring as the result of the development of new antibodies which could not have been detected or predicted pre-transfusion. However, in the cases in which early post-transfusion reactions occurred there is evidence that antibodies may have been present in some cases and "masked" by other antibodies in the sample.

- As in earlier SHOT reports the antibodies responsible for the DHTRs were consistent with those reported in the literature[10] with a preponderance of Kidd 14/34 (41%) of all antibodies, 14/30 (45%) of patients.

- In 7 cases there was no evidence of any haemolysis and patients were reported because of the later detection of new antibodies. This included one case detected to have anti-K 75 days post-transfusion. It is not the intention of SHOT to collect reports on allo-immunisation in the absence of other manifestations of DHTR although there may be occasions (e.g. development of anti-D in a young female patient) in which a report to SHOT is appropriate.

- In 2 cases the presence of an anti-Kidd was known historically but either not communicated to the receiving hospital or retrieved from Blood Bank records. The antibody was not detectable on pre-transfusion testing.

- An enzyme-only anti-E was felt to be implicated in a fatal transfusion reaction. Enzyme-only antibodies are not generally felt to be clinically significant and therefore this case is both unusual and worrying. The reaction pattern of the antibody evolved over the week post-transfusion, becoming reactive by both enzyme and IAT techniques.

RECOMMENDATIONS

- Laboratories should ensure that any antibodies which may be masked by a detected antibody(ies) have been excluded by the use of additional panels and techniques (e.g. enzyme-treated cells).

- Historical transfusion details should be communicated by referring hospitals and retrieved from previous transfusion records, where available.

- Nursing and medical staff should ask patients whether or not they carry a red cell antibody card at the time of drawing blood for pre-transfusion testing. However, it is currently not routine practice in all areas to issue these cards and their value in improving transfusion safety has not been formally assessed.

- For laboratories who may feel that alternative technologies may have been able to detect an implicated antibody in the pre-transfusion sample the National External Quality Assurance Scheme (Blood Transfusion Laboratory Practice) can offer a range of technologies which may not be available locally.

10. TRANSFUSION-RELATED ACUTE LUNG INJURY

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

There were 17 initial reports, of which one was withdrawn as it was decided that the diagnosis was not TRALI, leaving 16 new cases. Questionnaires have so far been received on 15 of them, and on 1 further case initially reported last year.

Of these 16 cases, there were 8 men and 8 women, with a median age of 53. There were no cases in children. The cases are summarised in Table 20.
One of these cases was a patient receiving intravenous immunoglobulin as the only blood product exposure. This case does not strictly fall within SHOT's remit, as IgG is a licensed medicinal product. As such, complications should be reported to the Committee of Safety of Medicines through their 'Yellow Card ' system. However, it is included here for completeness.

There were 4 fatalities to which TRALI may have been contributory. All were patients who were already very ill, and in whom sudden deterioration in respiratory function occurred during or soon after transfusion. The clinicians reporting all 4 cases admitted that they could not be certain on clinical grounds whether the patient had TRALI or cardiac failure. The withdrawal of the case described above who was thought to have TRALI but later considered to have cardiac failure illustrates the difficulty. A definitive diagnosis of TRALI traditionally requires one of the donors to whom the patient was exposed to have positive serology for leucocyte antibodies; however this information is rarely available when the case is reported.

Diagnoses

Five patients were transfused for surgical procedures (2 coronary artery bypass, 1 cholecystectomy, 1 pleurectomy, 1 fractured femur), and 2 others had acute haemorrhage, including 1 post partum with placenta praevia.
Three patients were undergoing plasma exchange procedures for haemolytic uraemic syndrome/thrombotic thrombocytopenic purpura (1 following bone marrow transplantation).
Two further patients had unspecified haematological malignancy, 1 with haemolysis.
There was 1 case each of meningococcal septicaemia, chondrosarcoma, and angioimmunoblastic lymphoma and a further patient with 3 diagnoses:- cold haemagglutinin disease, myelodysplasia and sarcoidosis.

Six patients were transfused in the operating theatre or in high dependency/intensive care units, and the remainder on the ward.

Components transfused

Five patients received red cells alone, 3 received FFP alone (including a patient having cholecystectomy), and 1 received cryosupernatant alone (a TTP case). Other patients received combinations of components (RBC + FFP in 1 case; RBC + FFP + cryoprecipitate in 1 case; RBC + FFP + platelets in 3 cases). These 4 cases all were exposed to >20 donors each. A further case who received RBC + FFP + platelets + cryoprecipitate was exposed to approximately 60 donors.
The final case received IgG as the only blood product exposure.

Table 20 Clinical Features of TRALI Cases

CASE NO.	SEX/ AGE	DIAGNOSIS	WHERE TRANS-FUSED	COMPONENTS RECEIVED	PRE-EXISTING FACTORS	NEW FEATURES ASSOCIATED WITH TRANSFUSION	CHEST X-RAY	TREATMENT FOR TRALI	ADMITTED TO INTENSIVE CARE UNIT (ICU)	OUTCOME	WHY REPORTER CONSIDERED CASE TO BE TRALI
1.	M 65	Coronary artery bypass graft	Intensive care unit/ theatre	5 RBC 2 FFP 1 Plt pool	None	↓ blood pressure, ↓ p02, dyspnoea, no left ventricular failure	-	Methyl-prednisolone	Already on ICU	Recovered	Onset following transfusion. No cardiac problems.
2.	M 51	Chondrosarcoma	High dependency unit	1 RBC	None	Fever, dyspnoea. ↑ secretions with blood	-	Anti-histamine, hydrocortisone	On high dependency unit already	Recovered	↑ O2 requirements during transfusion. Improved when transfusion stopped.
3.	F 63	Angio-immunoblastic lymphoma	Ward	1 RBC	Cardiomegaly, congestive cardiac failure, pleural effusion	↓ blood pressure, dyspnoea, ↓ pO2, ↑ pCO2	Acute pulmonary oedema	Methyl-prednisolone + anti-histamine	Yes, but not ventilated	Died	Sudden onset during transfusion.
4.	M 18	Meningococcal septicaemia	Ward	2 FFP	Sepsis	↓ pO2	-	Not stated	Yes. ? ventilated	Recovered	Onset during transfusion
5.	F 31	Haemorrhage due to placenta praevia	Ward/ intensive care unit/ theatre	32 RBC 2 Plt pools 7 FFP 11 Cryo	None	↓ blood pressure, ↓ pO2	Bilateral pulmonary alveolar shadowing.	Not stated	Yes. Ventilated 1 day (Positive end expiratory pressure)	Recovered	Sudden onset during transfusion
6.	F 33	Thrombotic thrombocytopenic purpura post allogeneic bone marrow transplant	Ward	Cryosupernatant for plasma exchange	None	Dyspnoea. ↓ pO2	Bilateral pulmonary shadowing	Hydrocortisone	Yes. Continuous positive airways pressure. Not ventilated	Died	Sudden acute deterioration <6 hrs after transfusion.
7.	F 60	Myelodysplastic syndrome, cold haemagglutinin disease, sarcoid	Ward	1 Red cell 3 RBC, BCD	None	Fits, right-sided weakness, dyspnoea. ↓ pO2	Bilateral fluffy shadowing	Anti-convulsants	No	Recovered	Sudden onset following transfusion.
8.	F 55	Cholecystectomy	Ward	FFP	Pulmonary hypertension. Cryptogenic fibrosing alveolitis, hypertension	Temperature ↓ then ↑.	Pulmonary `white out` suggestive of pulmonary oedema.	Frusemide, salbutamol, hydrocortisone, methyl prednisolone.	No, but 100% pO2 8 days.	Recovered	Sudden onset during transfusion.

Table 20 (continued) Clinical Features of TRALI Cases

CASE NO.	SEX/ AGE	DIAGNOSIS	WHERE TRANS-FUSED	COMPONENTS RECEIVED	PRE-EXISTING FACTORS	NEW FEATURES ASSOCIATED WITH TRANSFUSION	CHEST X-RAY	TREATMENT FOR TRALI	ADMITTED TO ICU	OUTCOME	WHY REPORTER CONSIDERED CASE TO BE TRALI
9.	M 27	Fractured femur	Theatre	1 RBC	Asthma	Fever, dyspnoea. pO2 97%.	None	O2; More blood.	No	Recovered	Not stated.
10.	M 68	Haematological malignancy	Ward	2 RBC LD 3 Plt pools 4 FFP	Ischaemic heart disease	Fever, dyspnoea, ↓ pO2	Mid-zonal bilateral consolidation.	Antibiotics, diuretics, dexamethasone.	Not thought appropriate	Died	`May have been cardiac failure`
11.	M 73	Pleurectomy for recurrent pneumothorax	Intensive care unit	10 RBC 2 FFP 12 Cryo	Respiratory dysfunction	Dyspnoea	Not stated	Not stated.	Already on ICU	Not stated – Notes missing.	
12.	M 40	Haematological malignancy; autoimmune haemolysis	Ward	25 grams IV IgG	Dyspnoea, sepsis	Fever, ↓ blood pressure, dyspnoea, ↓ pO2	Extensive alveolar shadowing	Methyl prednisolone	Ventilated for 40 days	Recovering	Unclear cause – 2 days post-transfusion.
13.	M 18	Haemolytic uraemic syndrome	Ward	3 FFP	None	Fever, dyspnoea, ↓ pO2, ↑ pC02	Consistent with pulmonary oedema	None	Ventilated 5 days	Recovered	Young fit patient; sudden onset following transfusion.
14.	M 64	Unstable angina. Coronary artery by pass graft, post-op bleeding	Intensive care unit/ theatre	6 RBC 8 RBC BCD 1 Plt pool 7 FFP	Cardiac failure	↓ blood pressure, ↓ pO2, ↑ pCO2	Severe bilateral pulmonary oedema	-	Ventilated	Died. *Post mortem: Lungs consistent with adult respiratory distress syndrome.*	Patient already ill – massive pulmonary oedema with low right atrial pressure. No evidence that this was left ventricular failure.
15.	F 38	Thrombotic thrombocytopenic purpura	Ward	3 RBC LD 4 FFP	None	Fever; ↓ blood pressure, dyspnoea, ↓ pO2,	Bilateral widespread alveolar shadowing	Dexamethasone	No	Recovered	Clinically not like left ventricular failure.
16.	F 33	Haemorrhage	Ward	6 RBC	None	↓ blood pressure, dyspnoea, ↓ pO2	Perihilar infiltrate and lower lobe shadowing.	Anti-histamine, hydrocortisone, salbutamol.	Yes, but not ventilated	Recovered	Onset 15 minutes post-transfusion.

Pre-disposing factors

There were none in 8 cases, with the remainder having sepsis (1), asthma (1), pulmonary hypertension/cryptogenic fibrosing alveolitis (1), ischaemic heart disease (1), respiratory dysfunction (2), and cardiac failure(2), 1 of whom had a pleural effusion.

Clinical features (see Table 20)

All had dyspnoea with reduced pO_2 compared to previous levels; 3 also had raised pCO_2.
Hypotension was a feature in 7 cases, fever in 6, and fits in 1 (not the TTP case).
A chest X ray was available in 11 cases. All showed diffuse fluffy perihilar shadowing, radiating out to the peripheries. In 1 case the chest x ray was described as 'pulmonary white out/pulmonary oedema'

Treatment and outcome

Nine patients received steroids in the form of either methylprednisolone, hydrocortisone, or dexamethasone.
Additional treatments were:- salbutamol in 2 cases, antihistamines in 3, diuretics in 1, antibiotics in 1 and anti-convulsants in 1.
Three patients were already on intensive care/high dependency units when transfused. A further 8 were admitted to ITU, of whom 6 were either ventilated or had continuous positive airways pressure. In 1 case, a 68 year old man with haematological malignancy, admission to ITU was not thought appropriate. Four cases did not require ITU admission, and were treated with oxygen therapy on the ward.

Four patients died following sudden deterioration in respiratory function during or soon after transfusion. One was the patient with underlying haematological malignancy not admitted to ITU; one was a 64 year old man with unstable angina who was transfused following coronary artery bypass surgery; one was a 33-year old woman who was undergoing plasma exchange for thrombotic thrombocytopenic purpura following a bone marrow transplant, and the fourth was a 63 year old woman with angioimmunoblastic lymphoma.

All other patients recovered fully.

The serological investigations on the patients and their donors are summarised in Table 21

COMMENTARY

- Over the 3 year period SHOT has been running, there have been a total of 43 reported cases of TRALI. Of these, 6 have been fatal, and a further 23 have required ITU care. If all such cases truly had TRALI as a sole or contributory factor to their outcome, this total of 29 cases makes TRALI the second most common cause of death/ITU care following transfusion after ABO incompatibility.

- The case definition we have used does not require positive donor serology. TRALI may be difficult to diagnose clinically. In reported cases, TRALI has been suspected because of a deterioration in respiratory function associated with transfusion. Not all cases have been supported by serological evidence, although investigations were highly variable.

- Over 3 years, 14/43 cases (33%) were in patients who had received only red cells, without exposure to plasma-rich components. This is important in relation to strategies UK Transfusion Services might consider to minimise TRALI risk.

Table 21

Leucocyte antibody investigations in 16 TRALI cases

CASE	PATIENT RESULTS		DONOR RESULTS				
	LEUCOCYTE ANTIBODIES	HLA / GRANULOCYTE TYPE	NUMBER OF DONOR EXPOSURES	NUMBER TESTED	NUMBER POSITIVE	RESULTS ON POSITIVE DONORS	COMPONENTS DONATED BY POSITIVE DONORS
1.	Nil in serum. ? IgG and IgM on granulocytes	A3, A31; B8, B50	8	8	1	Anti-HLA B7, B8, B15, B40 by LCT. Positive cross-match	FFP Female donor withdrawn from panel.
2.		Not tested	1	1	1	IgM anti-granulocyte. Abs by GIFT. Granulocyte IgG: Negative. HLA ab: Negative Cross-match: Not performed	Red cells. Donor withdrawn.
3.				Not	Provided		
4.	Negative		2	2	1	Lymphocyte reactive Abs	FFP. Donor withdrawn.
5.	No investigations performed since 52 donors implicated.						
6.	Negative	Not done	Multiple (plasma exchange)	Donor samples not provided to investigating laboratory.			
7.	Not done		4	4	0	-	-
8.	HLA Class I antibodies in serum; ? granulocyte and lymphocyte-associated IGM	NA1-, NA2+, NB1+, 5b+	4	4	4	2 donors had HLA Class I Ab, with 1 giving a positive granulocyte cross-match. 1 donor had IgM anti-NA1 but negative cross-match. 1 donor had granulocyte-specific IgG and IgM with positive cross-match. All lymphocyte cross-matches were negative.	All FFP. All donors parous females.
9.	Not done		1	1	1	Negative	
10.	Not done		9	3	2	Both had granulocyte antibodies. No cross-match done.	Both FFP; 1 male, 1 female.

Table 21 (continued)

Leucocyte antibody investigations in 16 TRALI cases

CASE	PATIENT RESULTS		DONOR RESULTS				
	LEUCOCYTE ANTIBODIES	HLA / GRANULOCYTE TYPE	NUMBER OF DONOR EXPOSURES	NUMBER TESTED	NUMBER POSITIVE	RESULTS ON POSITIVE DONORS	COMPONENTS DONATED BY POSITIVE DONORS
11.	Patient's granulocytes coated with IgG. IgG and IgM granulocyte Abs in serum.	Not tested.	24	24 (archive samples only)		All negative for HLA Abs. All positive for granulocyte antibodies – probably false reactions. Lymphocyte cross-match – negative. Granulocyte cross-match – positive, but possibly due to pre-coated cells.	Not possible to implicate specific donors/components.
12.				Not	provided		
13.	Not done		3	3	1	HLA antibodies. No cross-match done	FFP; female donor.
14.	Negative	HLA A2, A31; B7, B27	34	26 (7 pending)	2	Strong anti-A2 (probable cause) Strong anti-B17	FFP; female donor FFP; female donor.
15.				Not	provided		
16.				Not	provided		

RECOMMENDATIONS

- UK Transfusion Services should consider possible strategies for prevention of TRALI. This recommendation needs to be considered in its broadest aspects, including an option appraisal of different approaches to donor selection/screening, logistics, effect on the blood supply and cost-effectiveness.

- In particular, a view should be taken regarding the importance of TRALI prevention in relation to other priorities for further improvements in blood safety. This can only be achieved through a decision making structure which has the all the necessary professional representation including public health and health economics, to view new developments in blood safety in their overall context (see Chapter 16).

- A standard protocol for investigation of suspected TRALI cases is highly desirable.

11. 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.

There were 11 new reports of PTP. However, 1 was reported twice from different sources, making 10 new cases. Nine of these cases were female, and 1 male, with a median age of 65. There were no cases in children.
Questionnaires have so far been returned on 9 of these cases during this reporting year. Two questionnaires were also received on cases outstanding from last year (both females), making 11 cases to analyse fully. In one case, the serology did not fulfil the case definition as described above, but the case is included for completeness.
There was 1 fatality probably attributable to PTP, and a further death attributed to underlying carcinoma and leukaemia (in the same patient). All other patients made a full recovery.

A fatal case of PTP.

A seventy-nine- year old lady with 2 pregnancies in the distant past sustained a fractured neck of femur, and was transfused 3 units of red cells without fever or other acute reaction. Between 5 and 9 days later, her platelet count dropped to < 10 x 10^9/L. Investigations revealed that she was HPA-1a negative with HPA-1a antibodies. She was treated promptly with intravenous immunoglobulin (IVIg) and steroids but sustained an intracranial haemorrhage and died.

Diagnoses

Four cases had upper gastro-intestinal (GI) pathology : carcinoma of oesophagus (and acute myeloid leukaemia); oesophageal varices; gastritis/haemorrhage; GI bleed of unstated cause.

Six patients had transfusion for surgery, with 1 case each of : femoro-popliteal bypass; perforated appendix; total cystectomy and pelvic clearance; bilateral knee replacements; fractured neck of femur; axillobrachial embolectomy and vein graft.

One case was transfused for anaemia/menorrhagia.

Previous pregnancies/previous and current transfusions

The male patient had been previously transfused, as had 3 of the females.
All female cases had had previous pregnancies: 8 cases over 20 years prior to the transfusion, and 2 cases with a 5-20 year interval. None gave a history suggestive of fetal/neonatal alloimmune thrombocytopenia.

All patients had been transfused with red cells, generally 5-9 days prior to the onset of symptoms. Two patients had also received FFP. In the 6 cases where the information was given, 3 had an acute febrile reaction associated with the transfusion, and 3 did not.

Symptoms and platelet count

One patient, a 79 year old female with fractured neck of femur, sustained a fatal intra-cranial haemorrhage.
Two patients with pre-existing upper GI pathology had further GI haemorrhage.
One patient had macroscopic haematuria, and a further 5 had only minor haemorrhage and/or purpura.
In 2 patients, the thrombocytopenia was an incidental finding on a blood count (<10 x 10^9/L in 1, and 20-49 x 10^9/L in another).

The platelet nadir was < 10 x 10^9/L in 9 cases, and 20-49 x 10^9/L in 2 cases.

Specificity of platelet-specific allo-antibodies.

3 cases: HPA-1a alone

2 cases: HPA-1a and heparin associated antibodies (1 with axillo-brachial embolectomy and 1 with perforated appendix)

1 case: HPA-1a and- 3a

1 case: HPA-3a alone

1 case: HPA-1b alone (the previously transfused male)

1 case: HPA-1b and -3a (previous pregnancies and transfusions)

1 case: HPA-2b and Gov[b]

1 case: IgG antibody, with a laboratory report stating 'serology not supportive of PTP'

Treatment and outcome

One case received no treatment; 10 cases (including the fatality) received IVIg; 3 also received steroids. Two cases were transfused with random platelets and switched to HPA-1a negative platelets once the serology results were available.

One patient died of intracranial haemorrhage (having received IVIg and steroids), and one of underlying carcinoma of oesophagus/acute myeloid leukaemia. All others fully recovered, reaching a normal platelet count in a median of 4 days (range 2-21 days, with all except 1 recovering in < 12 days).

COMMENTARY

- This is the first year in which platelet alloantibodies combined with heparin-associated antibodies have been reported. As many as 50% of patients receiving heparin develop antibodies detectable by ELISA techniques, but ≤5% of those develop thrombocytopenia[6]. True heparin-induced thrombocytopenia is also often complicated by venous or arterial thrombosis not a feature in the 2 cases reported here. One of the 2 cases reported had a diagnosis of axillo-brachial embolectomy, but the report made no mention of in situ thrombosis occurring after heparin treatment. It is likely therefore that the heparin-associated antibodies were an incidental finding, and not the cause of the thrombocytopenia.

- The first case has also been received by SHOT which was clinically consistent with a diagnosis of PTP, but where the serology did not demonstrate a clear platelet alloantibody.

- All cases were treated appropriately and promptly with IVIg. There is no evidence that steroids offer any additional advantage. Similarly, transfusion with either selected or random donor platelets has not been proven to be beneficial; however, in an acutely haemorrhaging patient, it is often difficult to withhold platelet transfusion.

- There is almost certainly significant under-reporting of confirmed PTP cases to SHOT. The platelet immunology laboratory at East Anglian Blood Centre, which serves a population of approximately 13 million, identified 13 antibody-positive cases of PTP during a 2-year period (data kindly supplied by Mr C Hurd). It would therefore be expected that 20-30 confirmed cases/year would be diagnosed in the whole of UK and Ireland. In addition, PTP may be missed clinically, as shown by the 2 cases reported this year in whom it was an incidental finding. The true incidence may be much higher, although it is likely that most of these cases make a full recovery spontaneously.

RECOMMENDATIONS

- In patients diagnosed as having heparin-induced thrombocytopenia in whom there is no thrombosis, platelet-specific alloantibody investigations should be considered if the patient is parous or previously transfused.

- In patients with platelet-specific alloantibodies who require further red cell transfusions, units from donors lacking the relevant platelet alloantigen should be requested.

12. 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 3 new reports of TA-GVHD received during the reporting year. A fourth case transfused during the reporting year but notified later is also discussed for educational purposes, but for consistency will be included in next year's figures. Of these 4 initial reports, 2 questionnaires have been received and 2 are awaited (efforts are being made to obtain these). A further questionnaire on a case initially reported last year was also received, making 3 questionnaires to analyse.

Of the 4 new reports, 3 were male and 1 female, with a median age of 62 years. No cases were reported in children. All 4 cases were fatal, as has been the case with all 7 previous TA-GVHD cases reported in the past 2 years.

Of the 4 new reports, the underlying diagnosis/reason for transfusion was cardiac surgery in 2 cases, and myeloma in 1 case (questionnaire not yet received) with 1 as yet unknown. One case initially reported last year had Waldenstrom's macroglobulinaemia, and is fully described below.

No patient had received irradiated components, as none of the cases fulfilled the British Committee for Standards in Haematology's current criteria for their use[11]

Neither patient with a lymphoproliferative disorder had received purine antagonists.

Leucocyte depletion of the UK blood supply was gradually introduced during this reporting year. No patient with TA-GVHD had received leucocyte depleted blood components.

Case 1- Male, 74 years, with Waldenstrom's macroglobulinamia

This patient had previously been treated with vincristine, prednisolone, and cyclophosphamide.
He received a total of 7 units of non-leucocyte depleted red cells, the age of which was not stated.
Between 15 and 19 days after his transfusions, he developed a rash, diarrhoea, deranged liver function, pancytopenia, and a probable infection. A skin biopsy was consistent with GVHD.
He received full supportive care within 3 days of diagnosis but died from infection.

The patient's HLA type was not determined. Of 3 donors tested, one was homoyzgous:-
HLA: A1; B8; Cw7; DR17 (3), DQ2.
Thus TA-GVHD in this case may have been due to a possible HLA haplotype share between the patient and an HLA homozygous donor. Immunosuppression due to Waldenstrom's macroglobulinaemia and its treatment was a possible contributing factor.

Case 2 – Male 67 years, post cardiac surgery for coronary artery disease.

The patient had no pre-existing risk factors for TA-GVHD.

Peri- and post-operatively, he received 11 units of red cells, 4 doses of platelets (1 apheresis, 3 pools), and 8 units of fresh frozen plasma, and was thus exposed to 32 donors. Most of these components were given 20 days before the onset of symptoms; 2 units were given 11 days before onset. There was no suggestion that 'fresh blood' had been used for any of the transfusions.

Following the development of a rash, abnormal liver function tests and pancytopenia, a skin biopsy was performed. This showed T cell infiltration, but DNA could not be isolated from the sample. Bone marrow aspirate showed an aplastic picture. He received appropriate supportive care within 3 days from diagnosis, but died 8 days later from multiorgan failure.
Because of the large numbers of donors involved, HLA typing investigations were not done.

Case 3- Male 62 years, post cardiac surgery for coronary artery disease.

This patient had no underlying risk factors for TA-GVHD.

He received 2 units of non-leucocyte depleted, non-buffy coat depleted red cells –1 was 9-11 days old when transfused, the other was 14-16 days old.

He subsequently developed a rash, liver dysfunction, respiratory problems, and pancytopenia.

Tissue typing investigations revealed:-

Patient: HLA A3,33; B8,65; Cw7,8; DR7,17; DQ 2,9.
Donor 1: homozygous HLA A1; B8; Cw7; DR 17; DQ2.
Donor 2:HLA: A2,30; B18,35; Cw4,5; DR1,17; DQ2,5.

This demonstrates a partial haplotype share between the patient and the homozygous donor 1.

A skin biopsy of affected and unaffected skin was performed. Using variable number tandem repeat analysis on DNA extracted from peripheral blood and skin, sequences from donor 1 were found in affected skin and peripheral blood.

He received methyl prednislone and anti-lymphocyte globulin beginning 4-7 days after the onset of symptoms, but died 4 weeks after transfusion from infection.

COMMENTARY

- TA-GVHD remains a rare complication of transfusion, with 3-4 reports annually for the last 3 years. It is disappointing that questionnaires giving a full description of the case have been received for only 2 of the 4 new cases.

- There was 1 new case in a patient with B cell malignancy (myeloma), to add to the 2 cases in each of the 2 previous years. These previous cases were the Waldenstrom's macroglobulinaemia case analysed in this year's report, and 3 cases of B cell non-Hodgkin's lymphoma, none of whom had received purine antagonists. The BCSH Clinical Task Force is currently considering the issue of provision of gamma irradiated blood for all lymphoma patients.

- There were 2 new cases associated with cardiac surgery to add to the single case reported last year. Only 1 of these 3 cases was transfused with 'fresh' blood. In the 2 cases where HLA typing was performed, a homozygous donor sharing a complete or partial haplotype with the patient was identified. Cardiac surgery has been recognised in Japan as a risk factor for TA-GVHD. This raises the possibility that there is a second specific risk factor (in addition to HLA haplotype sharing) which pre-disposes cardiac surgery patients to TA-GVHD. However, no such risk factor has yet been identified.

- There were no cases of TA-GVHD due to failure to prescribe irradiated components for high risk patients. However, as outlined in Chapter 7, there were 7 episodes in which patients who should have received irradiated blood did not. This was the commonest prescribing error seen.

- There were no cases in which gamma irradiated components had failed to prevent TA-GVHD in at risk patients.

- None of the reported cases received leucocyte depleted components. Any possible impact of universal leucocyte depletion of the blood supply (achieved in November 1999) on TA-GVHD incidence will take several years of further monitoring to emerge.

- There is no recognised effective therapy for TA-GVHD.

RECOMMENDATIONS

- Patients at risk of TA-GVHD who are receiving shared care between a transplant/oncology centre and their referring hospital should carry a card to indicate their need for irradiated components. The possibility of a national standard card is being investigated.

- A standard protocol for the investigation of suspected TA-GVHD cases should be developed.

13. TRANSFUSION-TRANSMITTED INFECTIONS

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. 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 (PTI) may be due to an infected (or contaminated) transfusion or infection 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 British Isles (excluding Scotland) and the Republic of Ireland by the National Blood Authority and the Public Health Laboratory Service Communicable Disease Surveillance Centre (PHLS CDSC) in October 1995.

Retrospective data were collated in Scotland for cases occurring in Scotland during this year.

Methods

Participating blood centres (see above) reported all post-transfusion infections of which they had been informed to the NBA/PHLS CDSC infection surveillance system. 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/DNA 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 HAV, HBV, HCV, EBV or CMV infection in post-transfusion samples to date).

One category of post-transfusion infections is not included in these data. In January 1999, a meeting of reporters agreed that HCV and 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 should be excluded from reporting. The blood service is rarely able to conduct follow-up investigation of donors implicated in these cases and these cases do not contribute to knowledge of the current infection transmission risks of blood transfusions. Numbers and details of such infections are therefore not included in this report.

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)

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

Twice this year, all participating blood centres were reminded of the requirement to report, and asked to report any cases that had not yet been notified.

Data received by 31/12/99 about incidents of transfusion-transmitted infections initially reported by blood centres between 1/10/98 and 30/9/99 were included in this report. Data received about incidents reported during the previous three years of the surveillance system are included in a cumulative table.

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.

Results

34 initial reports of post-transfusion infections were made by blood centres during the report year. An additional 11 reports were received about post-transfusion reactions that were suspected to be due to bacteria but for which no evidence of bacterial infection (or endotoxin) that could have caused the reaction was sought and found in the recipient or implicated component (i.e. the incidents did not satisfy the criteria for a post-transfusion infection as stated above, but may have been reactions of bacterial origin). Reports were received from 12 of the 21 blood centres participating in the surveillance system. These 12 centres collect approximately 86% of the donations tested by blood centres participating in the surveillance system.
Figure 13 shows the classification of reports during the report year.
Of the 34 post-transfusion infections initially reported by blood centres to the surveillance system between 1/10/98 and 30/9/99, 7 (21%) were classified, after appropriate investigation, as transfusion-transmitted infections. Table 22 shows the transfusion-transmitted infections reported to the surveillance system between 1/10/98 and 30/9/99 by year of transfusion: Four were transfused during the report year, and 3 were transfused prior to the report year.

Figure 13
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 1/10/98 and 30/9/99.

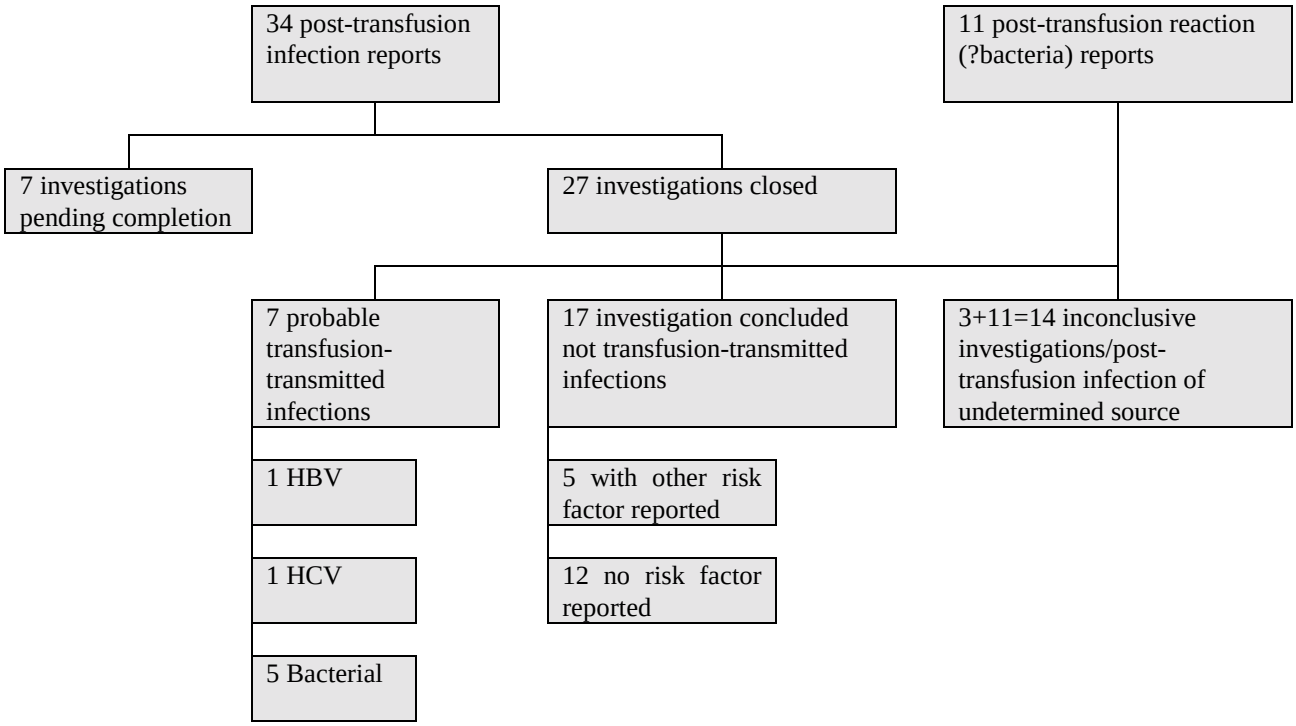


Table 22
Transfusion-transmitted infections reported between 1/10/98-30/9/99 by year of transfusion. The number of incidents are shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	1997	1998	1999 (to end Sept)	Total
Infection				
HBV	-	1(1)	-	1(1)
HCV	1(1)	-	-	1(1)
Bacteria	-	2(2) [a]	3(3) [a]	5(5) [ax2]
Total [b]	1(1)	3(3) [a]	3(3) [a]	7(7) [ax2]

Notes: [a] Infection was implicated in the death of a recipient.
[b] Additionally, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

A retrospective collation of cases investigated by blood centres in Scotland found three post-transfusion infection investigations during the report year. One recipient (72 year old male) developed pryexia and tachycardia after transfusion with red cells (23 days old, not leucodepleted). The recipient responded to antibiotic therapy and recovered. Coagulase negative *Staphyloccocus* was cultured from the red cell pack. For two post-transfusion HCV infection reports (one transfused in 1996, one in 1999) investigation was completed and no evidence was found to implicate transfusion as the source of infection. A probable source of infection other than transfusion was known for one of these cases.

Details of transfusion-transmitted infections

A. Infections for which donation testing is mandatory

Hepatitis B virus

One transfusion-transmitted HBV infection was reported.

One recipient (73 year old female) was found to have markers of acute HBV infection four months after transfusion of a red cell unit (one of three units received during a month) collected from a donor who developed acute HBV infection between one and two months after donating blood. The recipient was traced after the donor's General Practitioner informed the blood service of the donor's infection status. The archive of the implicated donation was confirmed to be HBsAg negative on re-testing but was found to be HBV DNA positive by nested PCR. (DNA was not detectable by PCR on a 1 in 96 dilution). The recipient died three months after her HBV diagnosis from the underlying reason for transfusion: HBV infection was not implicated in the recipient's death.

The probable source of the recipient's HBV infection was concluded to be an HBV infectious, though HBsAg negative, donation collected from a repeat donor during early acute infection. The blood donor did not report any risk factor for HBV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

Hepatitis C virus

One transfusion-transmitted HCV infection was reported. A repeat donor was found to be anti-HCV positive and HCV RNA positive. The archived sample of the previous (first) donation from this donor was re-tested and was also anti-HCV and HCV RNA positive. The recipient (a 64 year old male) of this red cell unit was traced and tested fourteen months after transfusion and was found to be anti-HCV positive and HCV RNA positive. Investigation by the blood service found an error had occurred during the re-testing of the donation that was initially reactive to the anti-HCV test. The duplicate repeat tests were read as negative because the samples were unintentionally dispensed into blank wells that are used to fill out part plates so they can be handled by automated machinery. It had been common practice to blank these out with a black marker pen to ensure that in the event they were accidentally used for samples they would return a fail safe positive reaction. However new machinery had been introduced which read these as negative. Once the problem was identified corrective and preventative action was put in place to ensure that a different mechanism is used to ensure that blank wells will if accidentally used return a positive result and "fail safe".

The probable source of the recipient's HCV infection was concluded to be an HCV infectious, anti-HCV positive, donation from a new donor. The donation was not excluded from the blood supply because of a laboratory error during the testing process. The blood donor did not report any risk factor for HCV infection that is currently included in the criteria for the exclusion of individuals from donating blood.

HIV

No transfusion transmitted HIV infections were reported during this year.

B. Infections for which donation testing is not mandatory

Bacteria

Five transfusion-transmitted bacteraemias were reported.

One recipient (27 year old male) developed bacteraemia after transfusion with two leucodepleted, 4 day old apheresis platelet units from the same donor. The recipient recovered and was asymptomatic one week after the transfusion. *Staphylococcus epidermidis* was isolated from the platelet packs and from the recipient (and these two isolates had identical banding patterns). *Staph. epidermidis* (with a different DNA fingerprint) was subsequently cultured from swabs of the donor's arms. *Staph. epidermidis* was not grown from swabs taken after standard skin preparation. No failure in the donor arm cleansing procedure at the time of donating the implicated donation had been noted.

The probable source of the recipient's bacteraemia was concluded to be transfusion with platelets contaminated with skin flora from the donor's arm.

One recipient (52 year old male) suffered a severe febrile reaction during transfusion of a leucodepleted, 3 day old apheresis platelet unit, and died later the same afternoon. On inspection the

next day the remainder of the platelet pack had some signs of bacterial contamination (unusual orange colouration and small specks visible when held up to the light). *Escherichia coli* was cultured from the recipient's blood and from the platelet pack (and these two isolates had identical biochemical profiles). No leaks or defects were identified in the platelet pack. An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs of the donor's arm skin were negative on culture.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with platelets contaminated with *E.coli*. No source of the contamination was identified.

One recipient (78 year old female) suffered symptoms including feeling hot, sweaty and dyspnoeic during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient subsequently recovered and was completely asymptomatic two weeks after the transfusion. Blood cultures were not taken from the recipient. *Staphylococcus epidermidis* was cultured from the platelet pack and from the red cell unit made from the same donation.
An interview with the donor confirmed absence of symptoms of infection at and around the time of donation and swabs from the skin of the donor's arm were negative on culture.
The probable source of the recipient's transient reaction was concluded to be transfusion with platelets contaminated with *Staph. epidermidis*. No source of the contamination was identified.

One recipient (63 year old female) developed urticaria, rigors and pyrexia during transfusion of a pooled, leucodepleted, 4 day old platelet unit. The recipient was pyrexial for three days after transfusion and was treated with broad spectrum antibiotics. *Bacillus cereus* was cultured from the recipient's blood and from the platelet pack (and these two isolates were both of type 29). *B cereus* (type 29) was also cultured from swabs from the skin of the donor's arm (both pre- and post- arm cleansing).
The probable source of the recipient's reaction was concluded to be transfusion with platelets contaminated with *B. cereus* from the donor's arm.

N.B. The above four cases were associated with leucocyte depleted platelets: all platelets issued in the UK since January 1999 have been leucocyte depleted. The numbers of cases are too small to detect any effect of leucodepletion on bacterial contamination of components.

One recipient (58 year old female) suffered a respiratory and cardiac arrest during transfusion of a second unit of red cells (33 day old, not leucodepleted) and died the same day. *Yersinia entercolitica* (serotype 09, biotype 3) was isolated from the patient's blood, the implicated red cell pack, the archive of the implicated donation and a fresh sample of blood taken from the donor 5 months after the donation. On follow-up the donor reported a history of diarrhoea a few weeks prior to the donation.
The probable source of the recipient's reaction, and cause of death, was concluded to be transfusion with red cells contaminated with *Yersinia entercolitica* from the donor's blood.

Details of post-transfusion infections not found to be transfusion-transmitted infections

Three (9%) post-transfusion infections (all bacteraemias) were classified as post-transfusion infections of undetermined source due to inconclusive investigation of the transfusion(s) implicated as the source of infection. For seventeen (50%) post-transfusion infection reports (1 HAV infection, 5 HBV infections, 7 HCV infections, 2 HIV infections, 1 syphilis infection and 1 bacteraemia), investigation was completed and no evidence was found to implicate transfusion as the source of infection. A possible source of infection other than transfusion was known for 5 of these infections (HBVx1: invasive medical procedure abroad, HCVx1: renal dialysis & transplant, HCVx1: tattoo, HIVx2: sexual risk factors).

Reporting delay

For the 5 transfusion-transmitted bacterial infections, disease occurred on the same day as the transfusion. Both of the transfusion-transmitted viral infections (1 HBV and 1 HCV) were diagnosed with sub-clinical infections (130 days and 440 days after transfusion respectively) during the follow up of suspected infectious donations. Blood centres were informed of the bacteraemias suspected to be associated with transfusion on the same day (3 cases), the next day, and 7 days after transfusion. The intervals between the blood centre being informed and the completion of the initial surveillance report form (i.e. reporting delay) were 124 days, 98 days, 32 days, 22 days and 12 days for the 5 clinically detected (bacterial) infections. The average interval between transfusion and the initial report (i.e. including all time intervals and reporting delays) was 135 days (n=7).

Under-reporting

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 under-reporting 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 year

During the previous reporting year (i.e. 1/10/97 to 30/9/98) 4 transfusion-transmitted infections were reported (see SHOT Annual Report 1997-98 for details of these cases). One of these was an HCV infection transmitted by transfusion prior to anti-HCV testing of blood donations: this case has now been excluded from the cumulative figures. None of the post-transfusion infections reported during the 1997-98 year that were pending full investigation at the time of the last (i.e. 1997-98) SHOT annual report have been subsequently concluded to have been transfusion-transmitted infections.

The investigations of seven post-transfusion infections that were classified as pending full investigation in the 1997-98 SHOT report have subsequently been concluded to be not due to transfusion (4 cases) or inconclusive (3 cases). One of the inconclusive cases concerned an HIV infection in a patient who had received multiple transfusions during the early 1990s and had no other risk factors for HIV infection. Investigation of the transfusions given to this patient did not identify a source of infection, however, as not all transfusions were investigated, transfusion with HIV infectious, anti-HIV tested, blood was concluded to be the probable, although unproven, source of infection.
Table 23 shows the cumulative number of transfusion-transmitted infections reported by the end of September 1999.
Figure 14 shows the number of reports received by year of transfusion since October 1995.

Table 23

Cumulative total transfusion-transmitted infections: reported between 1/10/95-30/9/99 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 (to end Sept)	Total	Deaths
Infection								
HAV	-	-	1(1)	-	-	-	1(1)	
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)-		5(5)	
HCV	-	-	1(1)	1(1)	-		2(2)	
HIV[c]	-	-	1(3)	-	-	-	1(3)	
Bacteria	-	1(1)	1(1)	3(3)	3(3)[ax2]	3(3)[a]	11(11)	3
Malaria	-	-	-	1(1)[a]	-	-	1(1)	1
Total[d]	1(1)[b]	2(2)	5(7)	6(6)[a]	4(4)[ax2]	3(3)[a]	21(23)	4

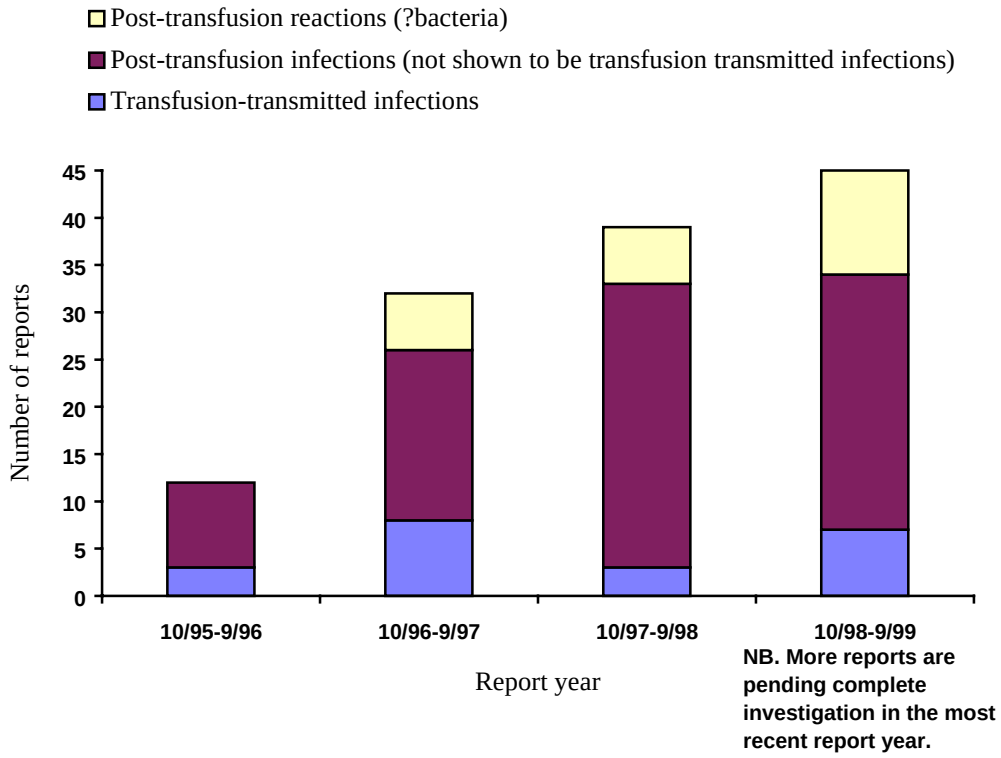
Notes: [a] Infection was implicated in the death of a recipient.

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

[c] One additional investigation, initially reported during 97-98 and concluded during 98-99, 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.

[d] Additionally, one probable transfusion transmitted bacteraemia (not fatal), transfused during 1998, was reported in Scotland.

Figure 14
PTI reports by report year



COMMENTARY

- Reported transfusion-transmitted infections are rare: only 7 confirmed cases were recognised during this 12-month period of reporting. Investigations of a further 29 cases of post-transfusion infection were reported. 50% of the PTI reports during this year have been shown not to be caused by transfusion. For 9% of the reports the investigation was inconclusive and for the remainder investigation continues. Similarly, in Scotland during this year, one probable case was recognised and two reports were shown not to be caused by transfusion.

- Eleven cases of post-transfusion reactions suspected (but not confirmed) to be due to bacteria were also reported. 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.

- The intervals between transfusion and diagnosis of transfusion-transmitted infections were long - many weeks, months or years. Infections transmitted by transfusion between 1/10/98 and 30/9/99 will continue to be ascertained by the surveillance system as diagnoses are made in the future.

- Two transfusion-transmitted viral infections (1 HBV and 1 HCV) were detected by follow-up of recipients after the detection of infections in blood donors. In one case (HCV) the donor's infection was diagnosed by the blood service by the testing of a subsequent donation, and in the other case (HBV) the donor's GP informed the blood service of the donor's infection. Neither of these transfusion-transmitted infections had caused symptomatic, diagnosed disease in the recipients. One of these transfusion-transmitted infections (HBV) was due to a donation collected from a donor during the marker negative "window period" early in a recent infection. One (HCV) was due to a laboratory error resulting in a false negative test result. Neither of these donors reported risk factors.

- Five transfusion-transmitted bacterial infections arose from donations from donors with infections for which no routine microbiology testing is performed.

- One reported transfusion-transmitted infection resulted from errors in the microbiological testing, or release, of blood donations.

- Two transfusion-transmitted infections, both bacterial, reported during this year resulted in the death of the recipient.

- Several reports have been received of components that were observed to have visual signs of bacterial contamination before use, were not transfused, were sent for bacteriological investigation and were found to contain bacteria expected to cause disease in a recipient if transfused. Inspection of components, especially platelets, detected contamination and prevented morbidity in these incidents. Such inspection should continue to be encouraged. These reports indicate "near-miss" bacterial transmissions. The investigation of the source of the contamination in these cases can be as informative as the investigation of transmissions, and the possibility of requesting and collating some information about these cases in the future is being considered.

RECOMMENDATIONS

- Careful inspection of blood components can, in some cases, detect bacterial contamination and prevent potential transmission. Components showing any unusual colour, turbidity or clumping should not be transfused, but should be returned to the Hospital Blood Bank for culture.

- Clinicians should report all post-transfusion infections diagnosed in their patients to their regional blood service for appropriate investigation. Blood centres should, in turn, complete an initial report form as soon as possible.

- The quality of investigation of transfusion reactions suspected to be due to bacteria is variable. Hospitals should consult guidelines and the blood service about the investigation of such cases, including the sampling and storage of implicated units. National guidelines (from the NBS) on the investigation of these cases are currently being revised following comments from users.

- Donors' clinicians (and donors themselves) can aid the detection of transfusion-transmitted infections, and hence their appropriate care, by communicating with the blood service about any relevant history of blood donation on patients diagnosed with blood borne infections.

- National collation of data arising from these cases needs to continue over several years before a picture of the extent and nature of the infectious complications of transfusion can emerge.

14. NEAR MISS EVENTS

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

'Near Miss' events are recognised as a good indicator of strengths and weaknesses within a process. They often have the same root causes as actual transfusion accidents but their higher frequency allows systems to be analysed and corrected before accidents occur. The reporting of such events has created significant interest and enthusiasm to introduce a permanent reporting system for this area. A small pilot scheme was undertaken and reported in the 1997-1998 Annual Report. However to obtain more meaningful data and validate the trial findings a larger survey was required, so during the course of that reporting year hospitals returning a "nil to report" card were asked if they wished to express interest in taking part in a larger study. So many hospitals expressed interest that it was not possible to invite them all to contribute because of the greater frequency of "near miss" events and resource limitations in the SHOT office. Approximately 25 hospitals were chosen to take part in data collection, the choice being rather loosely based on size and type of hospital and geographical location to reflect a wide range of hospitals. Data collection commenced on 1st March 1999 and officially ran for 7 months. 22 hospitals eventually contributed and a further 26 reports that were received from a few hospitals, not invited to participate, were included in the analysis.

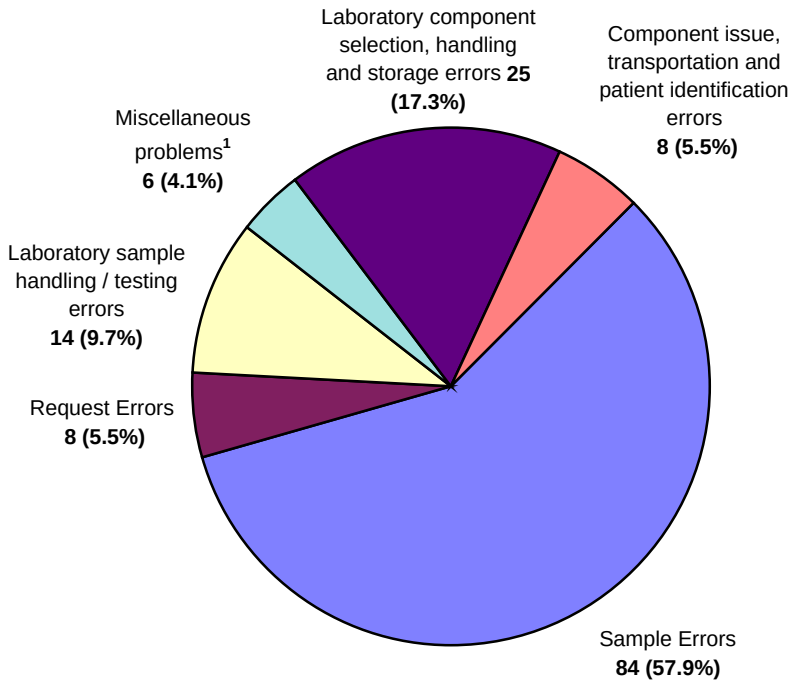
The potential for an error to have a serious consequence depends upon many factors, including the effectiveness of any subsequent checks built into the process. The first three years of SHOT reporting have shown that in many instances several errors may contribute to a "wrong blood" incident. Consequently what may be deemed to be minor errors may escape later recognition and play a significant role in a serious outcome.

To ensure a standard format and a simple method of recording problems, forms, mostly utilising tick boxes, were issued to all collaborating laboratories, with no follow-up questionnaires involved. This limited the amount of effort involved in completion of the information, but inevitably some details of the problems were missed. The 5 activity areas covered on the 'near miss' report forms are:

1. Sample errors
2. Request errors
3. Laboratory sample handling/testing errors
4. Laboratory component selection, handling and storage errors
5. Component issue, transportation and patient identification errors

Some incidents were also submitted which could not be classified into the defined 'near miss' categories and these are included as miscellaneous reports.

Figure 15
Categories of 'near miss' errors reported (N=145)



[1] Reports that did not meet the defined SHOT 'near miss' criteria

A total of 145 errors were reported between 1 March and 30 September 1999 and 139 have been evaluated (figure 15). Of these 6 were reports submitted where protocols within the individual hospitals were not followed, but where the errors involved did not fit the defined SHOT 'near miss' criteria, although they were of concern to the reporting hospital. These reports included an instance of blood being transfused without the laboratory report form and bedside checking could not, therefore, have been performed correctly.

Also among the 26 reports received from hospitals not invited to participate were 2 cases of inappropriate transfusion of blood components, which it would have been more appropriate to classify as IBCT incidents. These were a laboratory technical error giving a false negative antibody screen resulting in the transfusion of c positive red cells to a patient with anti-c, and the switching of patient compatibility labels between 2 patients, one of whom received the component, whilst the error with the other unit was detected during the bedside checking procedure.

Sample errors (84)

Poor phlebotomy procedures were the major problem in all reported 'near miss' events. Among the 84 reported incidents

- 24 samples were identified as being taken from the wrong patient.
- 44 were taken from the intended patient but labelled for another patient.
- At least one incident occurred when 2 patients' samples were switched.
- Other problems involved different patient identification details on samples and request form, and there were 9 cases where samples were received unlabelled. Although these samples would not have been used for testing, they are further examples of poor phlebotomy practices.
- The majority of samples was collected on the wards by medical staff (44), but nurses (16) and phlebotomists (5) were also involved.

- 50 errors were stated to have occurred during routine hours and 17 during on call or out of hours periods.
- At least 46 of the errors were detected within the laboratory by comparison with the historical patient record
- 6 of the problems were realised retrospectively by the person who performed the venepuncture
- Only 1 case was reported as involving the use of addressograph labels on the sample, but at least 5 of the problems were caused by the use of an incorrect label on the request form.

Request errors (8)

- 8 reports involved the lack of notification to the laboratory of the need to irradiate components for patients receiving the chemotherapy drug fludarabine, a purine analogue.

Laboratory sample handling and testing errors (14)

- In 5/14 cases an incorrect patient sample was used
- 5/14 reports involved clerical error leading to 4 incorrect blood group transcriptions.
- 3/14 reports were of technical errors and resulted in an incorrect RhD type, an incorrect ABO group and the wrong interpretation of a positive antibody screen.
- 10 errors occurred out of hours and 4 errors occurred during routine working hours.

Laboratory component selection, handling and storage (25)

- 9/25 errors were avoidable failures to select the correct component, the majority being a failure to provide CMV antibody negative components, the need for which was defined within the laboratory records.
- 6/25 were errors of incorrect labelling of components.
- 1 dose error in issuing platelets occurred. A request was received for 4 (single donor) bags of platelets but 4 adult therapeutic doses were issued.
- 7 errors of incorrect storage of components were reported, although all errors occurred within areas outside the direct control of the laboratory. These comprised:

  3 incidents of red cells found in ward domestic refrigerators
  1 unit of FFP stored for 12 hours in a ward domestic refrigerator
  1 unit of red cells put into a theatre domestic refrigerator
  1 platelet bag stored within theatre in a freezer
  1 unit of red cells placed in a bone bank freezer at -40°C

- 6/7 of the storage errors occurred outside normal laboratory hours, although only 10 of the 25 reports in this category were in this same time period.

Component issue, transportation and patient identification errors (8)

- 3 incidents were reported of the wrong patient's blood being taken to the ward or theatre.
- A unit of red cells was sent by ward staff to another hospital in a carrier bag.
- There were 2 reports of red cells being frozen during transportation:

  4 units of red cells were transported from a Blood Centre to a hospital laboratory in an insulated box with dry ice pellets. The red cells were received frozen.

  On the other occasion, red cells for a patient being transferred between hospitals, were sent in an insulated box containing ice inserts. The receiving nursing staff were concerned that the units appeared partly frozen and reported the problem to the laboratory. Upon centrifugation of the units that they were found to be grossly haemolysed.

COMMENTARY

- Incorrectly followed phlebotomy protocols were identified as the single major problem area in 'near miss' reports. Sample errors comprised 57.9% of all reports compared to 48% detected in the small pilot survey of 'near miss' events summarised in the 1997-1998 Annual Report.
  Incorrect samples taken from patients with the same blood group or samples from patients not previously tested are unlikely to be recognised, so approximately 50% of sample errors will remain undetected. In 2 unpublished studies in the UK, the frequency of incorrect phlebotomy has been estimated at approximately 1 per 3500 samples collected. The frequency of phlebotomy problems within individual hospitals in this project could not be ascertained because of the anonymous reporting mechanism, but evaluation of reports, using the workload data quoted on the forms, gives a possible error rate of just over 1 per 4000 samples received.

- Request errors were few but all involved failure to notify the laboratory of the need for irradiated components for patients being treated with purine analogues.

- Errors of laboratory sample handling and testing were lower than in the 1997/98 pilot study (9.7% compared to 25%) but nevertheless point to mistakes in clerical and technical tasks.

- Failure to select components with the correct special requirements, despite the presence of appropriate laboratory records, comprised 36% of laboratory component selection, handling and storage errors.

- Labelling errors occurred in the laboratory on 6 occasions (24% of component selection, handling and storage errors)

- Incorrect storage of components by non laboratory personnel outside the confines of the laboratory was reported on 10 occasions, 3 during transportation of components between sites.

- There were only 3 incidents of collection of the wrong blood from blood banks in contrast to the high incidence of this type of error in IBCT events where failure at this point was always followed by failure of the bedside check.

RECOMMENDATIONS

- Failure to follow phlebotomy protocols is a common cause of “near miss” events. The reasons for this should be identified and appropriate training given to all staff who undertake this procedure.

- Individuals responsible for ordering blood components must be familiar with the special needs of their patients, as emphasised in Chapter 7.

- Despite the rigorous standards which apply in most hospital blood banks there is a need for constant vigilance and regular review of competence in order to avoid clerical and technical errors.

- The laboratory record is an essential tool in ensuring correct component selection. This report suggests that it is sometimes ignored.

- There is a clear need to educate staff responsible for the handling of blood components as to their correct handling, storage and transport.

15. TOWARDS AN OVERARCHING VIEW OF BLOOD SAFETY IN THE UK

Background

Many countries in Europe and elsewhere are devoting considerable energy to the establishment of systems for 'haemovigilance', a term loosely applied to a process for monitoring and analysing transfusion hazards. In some countries (Germany, Canada), this has been followed by establishment of a body with overall responsibility for blood safety issues. With three years of reported cases now available, SHOT data provide a powerful body of evidence concerning current residual transfusion risks in the UK, which can be used to inform decisions taken around transfusion safety. It is therefore timely to consider the advantages which an overarching approach to blood safety would bring to the UK.

When SHOT was established, its Terms of Reference included the following 'Through the participating bodies, the information obtained will contribute to:-

a) improving the safety of the transfusion process
b) informing policy within Transfusion Services
c) improving standards of hospital transfusion practice
d) aiding production of clinical guidelines for the use of blood components.'

In considering how improvements to blood safety arising from the first two reports should be developed, it has become increasingly apparent that responsibility for the safety of blood components is spread across a large number of bodies, each dealing with one particular aspect (Figure 16). A number of initiatives have already been taken by some of these in response to the findings of the first two reports (Table 24), notably an urgently needed Guideline on blood administration published by the British Committee for Standards in Haematology. This 'piecemeal approach' has been acceptable so far, because 'wrong blood to patient' episodes, some of which are ABO incompatible, stand a long way ahead of others as the commonest transfusion hazard, and also as the commonest cause of death/ITU admission reported to SHOT. However, this problem is unlikely to be solved by attention to blood handling procedures alone. To reduce 'wrong blood' episodes to the vanishingly low level of viral transmission now seen, considerable investment in novel information technology systems would be required in every Trust, as has been undertaken in UK Blood Centres. At present, this decision would be a matter for local Trust management, opening up the possibility of different safety standards in individual Trusts around the country.

A further crucial issue is that the list of further possible safety steps is ever longer, including genome testing for viruses, virus inactivation of blood components, bacterial screening of platelets, extension of the indications for irradiated components to eliminate TA-GVHD, and donor selection or screening to reduce the incidence of TRALI, all of which compete for resources. It is essential that these new technologies be assessed by UK Transfusion Services for operational utility in case the emergence of new pathogens necessitates their rapid implementation. However, it must be recognised that, at the present time, introduction of many of these initiatives would have minimal impact on overall blood safety, and would not fulfil generally accepted criteria for medical cost-effectiveness. There are nevertheless considerable commercial pressures behind some of these new technologies and there is a real danger that resources will not be optimally directed if these possible developments are not considered within a broad single intellectual or administrative framework.

At present, no such framework exists, and decisions regarding implementation of any one of these further initiatives could in theory be taken by different responsible bodies without reference to the others (Table 25). At present, there is no common meeting point at which all proposals for further improvements in blood safety can be considered alongside each other.

Towards a possible solution

One model would be to create a unified body with overall responsibility for blood safety. Such a body would include representatives from the various organisations shown in Figure 16. Evidence from multiple sources on transfusion risks would be reviewed, and possible solutions and recommendations from individual groups considered. However, additional professional input from the Public Health and Health Economics communities would also be essential. The number of individuals transfused in the UK is somewhere in the order of 750,000/year, so that policy decisions on blood safety fall very well into the Public Health arena. Difficult though it may be, costs and cost-effectiveness must be considered at some point in the decision-making process. Health economic input will help to ensure that 'efforts are aligned with risks', even though the unattainable dream of a 'zero-risk' blood supply will never be with us. One important role of a decision-making body would be sometimes to decide that the risk of a given complication is already acceptably low compared with risks of other medical interventions, and that no further steps to reduce its incidence are necessary.

It should be noted that such an initiative would not be concerned with appropriate prescription of blood and components. This is an equally important and complementary element to decision taking in blood safety, but needs to be considered separately as there are different key players who should be included eg major blood prescribers such as anaesthetists.

Are there any drawbacks to taking an overview of blood safety?

Paradoxically, it is possible that creation of a single body with transfusion responsibilities may increase transfusion risks if a slow centralised decision-making process undertaking widespread consultation delays implementation of safety improvements. Ongoing dialogue with participating bodies will be important in ensuring timely decision-taking and action.

TABLE 24

RECENT INITIATIVES IN BLOOD SAFETY

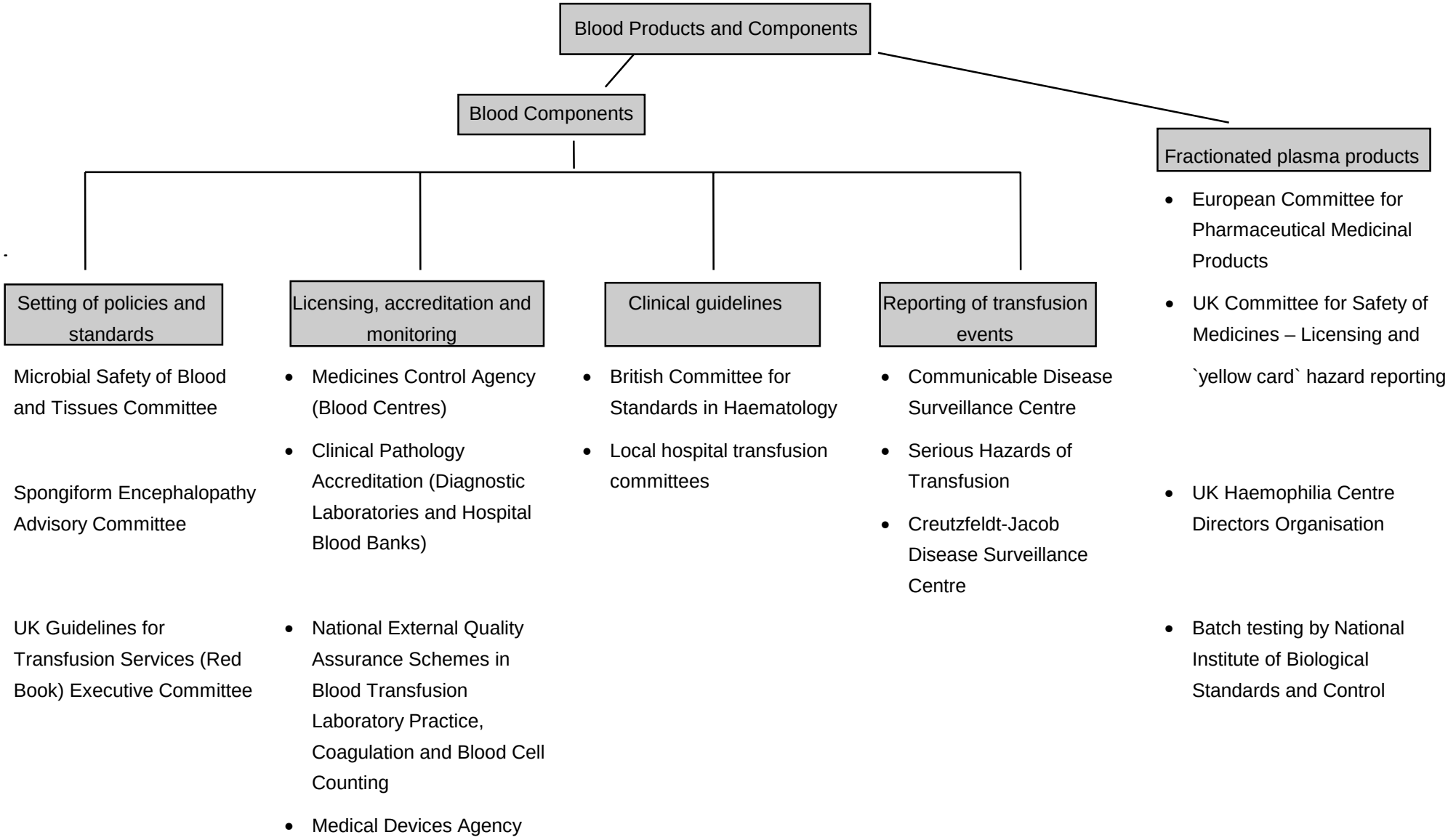
IMPROVEMENT	DECISION TAKEN BY:
Donor selection to exclude malaria	UK Transfusion Services
Direct donor questioning	UK Transfusion Services
Improved donor arm cleansing	UK Transfusion Services
Guideline on Blood Administration	BCSH
Requirement for hazard monitoring	CPA
Exercises to test red cell alloantibody detection	Red Cell Serology, NEQAS

TABLE 25

POTENTIAL FUTURE INITIATIVES IN BLOOD SAFETY

IMPROVEMENT	WOULD BE DECIDED BY:
Bar coded patient identification systems	Each Hospital Trust
Donor selection/donation screening to reduce TRALI	UK Transfusion Services
Bacterial screening of platelets	MSBT
Further indications for irradiated components	BCSH
Improved red cell serology	CPA/NEQAS

Figure 16
Organisations Contributing To Blood Safety In The United Kingdom



16. ACKNOWLEDGEMENTS

This is the third annual SHOT report and we are, once again, 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 report would not have been possible.

The Blood Transfusion Services of the United Kingdom and the Republic of Ireland

The British Society for Haematology

The British Blood Transfusion Society

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

Steve Carroll for Information Technology Services

Financial Services, NBS Northern Zone

Microbiological Reference Unit, SNBTS for information about post-transfusion infection reports in Scotland

Richard Lodge for the provision of data relating to the issue of blood components from the Transfusion Services of the UK and Ireland

Jane Costigan, SHOT office administrator

Blackwell Scientific Publications for permission to reproduce the Guideline shown in Appendix 8

All those hospitals who have participated in SHOT reporting

Without your support, SHOT would not be possible

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