SERIOUS HAZARDS OF TRANSFUSION **SHOT**

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Affiliated to the Royal College of Pathologists

British Blood Transfusion Society • British Society for Haematology
Faculty of Public Health Medicine • Institute of Biomedical Science
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

2. FOREWORD

Blood transfusion is a widely used therapy in hospital practice, with over 2 million units of red cells issued annually. Nevertheless, there has been a growing awareness among UK transfusion specialists, haematologists and other clinicians that there is little information on the current safety of the whole transfusion process from blood component production in a Transfusion Centre to administration at the bedside. Major policy decisions have had to be reached, and clinical guidelines produced, without a sound basis of epidemiological and statistical information. As suppliers of therapeutic products in the era of HIV, new hepatitis viruses and new variant Creutzfeld-Jacob Disease, Transfusion Services have an obligation to understand the magnitude of patient risk caused by their products. At hospital level, reports from the UK and elsewhere have suggested that errors in patient identification were a major source of transfusion-related morbidity and mortality.

These concerns culminated in the formation, in 1994, of a working group of hospital and transfusion service consultants, to produce proposals for the establishment of a UK-wide surveillance scheme for the reporting of major transfusion-related complications. A number of key questions had to be considered by the working group - was the scheme to be voluntary or mandatory, as in some other countries? What range of complications should be included? How was absolute confidentiality to be maintained? Who should 'own' the scheme, and pay for it?

The efforts of the Working Group finally came to fruition in November 1996, with the launch of the Serious Hazards of Transfusion scheme (SHOT), marked by an editorial in the British Medical Journal. SHOT's remit is to receive and collate confidential reports, sent on a voluntary basis, of transfusion-related deaths and major complications. The details of the scheme as it currently operates, are described on page 10-13, but it is appropriate at this point to acknowledge the tremendous support of the Steering Group established to oversee SHOT's activities. Transfusion is a complicated process, involving staff from a variety of professions and specialties. In recognition of this, the Steering Group includes representation from 8 Royal Colleges and 6 professional bodies, so that all staff who deliver blood components to patients have direct input to SHOT's policies and development.

Our endeavours were greatly helped by the fact that, in a parallel initiative, the Public Health Laboratory was working with the English National Blood Service, to centralise and improve the reporting of post-transfusion infections. This venture, though functionally separate, has been brought under the SHOT umbrella for this report, to provide a co-ordinated approach to publicising post-transfusion complications.

The gestation period of SHOT has been long, but the first year has proved that such a voluntary scheme can yield useful information. New initiatives within SHOT are planned, and we feel confident, that with your support, we can endeavour to maintain and improve the high standard of transfusion safety which the UK currently enjoys. We wish to thank all those of you who took the time and trouble to send in reports. We urge hospitals to help us make future reporting as complete as possible. Only in this way can a complete picture of transfusion risk emerge, and resources be directed to where most benefit will result.

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Chair, SHOT Steering Group

3. BACKGROUND

Serious Hazards of Transfusion initiative represents the first moves in the UK towards systematic haemovigilance. This is a broad term which has come to be used for any process by which morbidity and mortality arising from blood transfusion is monitored. A number of approaches to this process are possible, as the variety of systems in use in different countries illustrates[1,2]. Should reporting be voluntary or mandated by law, and what are the medico-legal implications? What range of complications should be included - fatalities and infection transmissions must obviously be covered, but would inclusion of minor reactions swamp the reporting system? What should be done to monitor 'near miss' events, where an error is discovered in time to prevent transfusion? Which blood derivatives should be included, given that licensed plasma products are already monitored by their licensing body? Should all patients be tested following transfusion for evidence of infection? Should the reporting scheme be 'owned' by the producers, or the users, and who should provide funding? These are only some of the issues to be addressed prior to establishing a haemovigilance system, and the solutions are not necessarily simple.

Nevertheless, the potential advantages of a haemovigilance system have probably never been greater. At this particular time, transfusion in the developed world is probably safer than it has ever been, although patient acceptance of risk in medical care appears to be decreasing. The Chief Medical Officer in England, Sir Kenneth Calman, has formulated a practical way of comparing medical risks with those in real life, which might prove useful in decision making (Table 1, modified from[3]).

Table 1. Description of Risk of Daily Activities

Term	Absolute Risk of Death in a Year	Example
High	>1:100	Intravenous drug use
Moderate	1:100-1,000	Smoking ten cigarettes a day
Low	1:1,000-10,000	Road traffic accident
Very low	1:10,000-100,000	Playing football
Minimal	1:100,000-1,000,000	Train accident
Negligible	<1:1,000,000	Struck by lightning

Further reductions in the viral risk of transfusion are promised by extremely expensive, well-marketed strategies such as virus inactivation of fresh frozen plasma and nucleic acid testing for viruses as a supplement to serological tests. At the same time, more stringent budgets lead blood bank managers towards multi-skilled or less qualified individuals, with computer cross-matching partially replacing laboratory testing. This, together with increasing pressures on clinical staff and the employment of temporary ward staff, make it increasingly important to establish the relative risks of the recognised complications of transfusion. This will help ensure that future spending can be wisely directed, and the impact of organisational changes on transfusion safety can be monitored.

The clinical transfusion process and its hazards - whose responsibility?

The complexity of the transfusion process has been graphically illustrated by the work of McClelland and colleagues[4]. A large number of people of varying professional training and knowledge are involved in the delivery of a safe unit of blood to a patient. These fall into three broad groups - the UK Transfusion Services, responsible for selection of donors, and for processing and testing of the unit; the hospital blood bank, responsible for component storage, selection and compatibility testing; and phlebotomy/portering/nursing staff responsible for withdrawing the crossmatch sample, delivering blood units from the laboratory to the ward, for administering the transfusion and for monitoring the patient. Medical staff are always responsible for prescribing blood components, although responsibility for ensuring that 'special requirements' are met, such as the need for irradiated, CMV negative, or leucocyte depleted blood is often delegated to the blood bank.

In the United Kingdom, regulation and training of these three bodies of staff is disparately controlled. Transfusion Centres, which in some parts of the UK also provide blood banking services, are required to hold Manufacturers (Specials) Licences from the Medicines Control Agency. Licensing is granted against compliance with Good Manufacturing Practice and the UK Guidelines for the Transfusion Services 'Red Book'[5], a document produced by the Transfusion Services of the four home nations in collaboration with the National Institute of Biological Standards and Control. Hospital blood banks can now gain accreditation through Clinical Pathology Accreditation, although this is not mandatory, and participate in the NEQAS serology scheme. In addition, the British Society for Haematology Transfusion Task Force produces a series of guideline documents covering both blood bank procedures and blood component prescription, some of which have an impact on manufacturing. Current guidelines include compatibility testing, neonatal transfusion, irradiated components, platelets and fresh frozen plasma[6-10], while a guideline on leucocyte depletion is nearing completion.

Decisions on microbiological testing of blood are taken at Department of Health level.

All this serves to underline the complex nature of 'responsibility' as applied to the transfusion process, and the need to involve all interested parties in any haemovigilance process. A brief review of the major complications of transfusion will illustrate this point further.

In the eyes of the public and many health care professionals, the major hazard of transfusion is transmission of infectious agents. Transfusion-transmitted viruses, particularly HIV and the hepatitis viruses (HBV, HCV, and more recently HAV and HGV), have been in the news for over a decade, and were primarily responsible for the growing interest in autologous transfusion. Add to that list parvovirus B19 and HTLV[11], and transfusion begins to appear a risky process. A recent study from the United States of America, however, demonstrates that the residual risk of HIV from transfusion is extremely low (1 in 500,000) and approximately 1 in 60,000 and 100,000 for HBV and HCV respectively[12]. Such risks depend on the background prevalence of viral carriage in the general population, and the testing strategy adopted. It should be noted that screening for hepatitis B core antibodies, HIV p24 antigen and antibodies to HTLV I/II are not mandatory tests in the UK. The addition of genomic detection for viruses to the current testing regime will further shorten the 'window period' during which a donor may be infectious but test negative.

The role of other infectious agents should not be forgotten. Fatal bacterial contamination of red cells occurs rarely but on a regular basis[13], while increasing attention has been drawn to the problem of bacterial contamination of platelets[14]. A recent WHO conference concluded that 'there has been no proven or even probable instance of transmission of Creutzfeldt Jakob disease from human to human by blood transfusion or blood products'[15]. A risk assessment is currently under way to examine the likelihood of new variant CJD being present in, and transmitted by, blood products.

Responsibility for preventing transfusion-transmitted infection virtually always lies solely with the supplying Blood Centre. Hospital staff have a preventative role in identifying bacterially contaminated units by inspecting packs for haemolysis. After the first of only two HIV transmissions in 12 years in the UK[16], it was ruled (in Scotland, at least) that responsibility could not be passed back to the donor, even if relevant life-style information was deliberately withheld.

The major cause of non-infectious transfusion fatality and morbidity is ABO incompatible transfusion, usually because blood intended for one patient is inadvertently given to another[1]. The frequency of 'wrong blood to patient' episodes has been estimated at 1 in 30,000 transfusions[17]. The mortality is minimised by the fact that, by chance, approximately two thirds of such incidents do not result in an incompatible transfusion, and because only 1 in 10 ABO incompatible transfusions are fatal[18]. 'Wrong blood to patient episodes' can arise because a cross-match sample is taken from the wrong patient, or labelled wrongly, because ABO grouping of the patient is incorrectly performed or interpreted, or because identity checks at the time of issue or administration of the blood are inadequate[19]. American data suggest that the frequency of this complication may be falling[20]. Other major immediate or delayed reactions may arise from laboratory failure to identify clinically significant red cell antibodies or to provide appropriate antigen-negative blood. Responsibility for this group of hazards lies almost always at the hospital level; ABO incompatibility due to a misgrouped donor unit is now extremely rare.

Other potentially fatal complications of transfusion include transfusion-associated graft-versus host disease (TA-GVHD), transfusion-related lung injury (TRALI) and post-transfusion purpura (PTP). TA-GVHD is preventable by gamma irradiation of cellular components to 25 Gy for susceptible patients. UK Guidelines are available, covering both clinical and manufacturing aspects [8]. Cases could therefore arise because of failure of clinical staff to request irradiated components, or inadequate irradiation procedures by the blood bank or supplier. Occasional cases arising in non-immunosuppressed individuals because of HLA haplotype sharing would be preventable only by universal component irradiation. TRALI arises because of interaction between the patient's leucocytes and strong HLA or granulocyte antibodies in donor plasma[21]. Such antibodies are most commonly seen in multiparous women.

PTP, in which profound thrombocytopenia follows 7-10 days after a red cell transfusion is virtually always seen in parous women, often elderly. The plasma of such patients contains alloantibodies to one or more alleles of the 9 Human Platelet Antigen (HPA) systems, usually HPA-1a[22].

The first year of the SHOT initiative has aimed to capture transfusion events relating to these complications. Details of how SHOT is organised are given in the next section of the report.

4. AIMS

The Serious Hazards of Transfusion (SHOT) scheme was launched in November 1996. SHOT is a voluntary anonymous 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.