II. Current risks associated with allogeneic blood transfusion

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In the developed world, with all-voluntary donations, self-exclusion and advanced screening assays, the risks of blood transfusion to recipients are very low. Although allogeneic blood transfusion has never been safer, the perception of the public, fed by the media, is that blood is becoming increasingly unsafe. Commercial companies are partly to blame for this distorted public perception because they are driven by the desire to increase the number and complexity of expensive screening tests and procedures with the justification that their participation will improve the safety of the blood supply. The reality is that any increased sophistication of testing or processes will accrue diminishing returns for considerably high costs. Because the current serious risks of blood transfusion are so low, it is difficult to quantify them and it is practically impossible to assess new measures to increase the safety of the blood supply. For example, there have only been 4 window period donations, with the possibility of transmitting HIV by transfusion in the UK since screening for anti-HIV started in 1985, i.e. 4 cases in > 45 million units of blood issued for transfusion.

The transmission of viruses by transfusion has led to measures to reduce the window period of infectivity, especially for HCV. PCR, or nucleic acid testing (NAT) of individual donations or plasma pools has been introduced for HCV (and HIV) in many countries, at considerable expense for very little return. For example, in England, since NAT was introduced, there have been 8 donations testing positive for HCV by NAT and negative for HCV antibodies by ELISA. Universal leucodepletion of blood components has also been introduced in many countries. It would not be surprising if photochemical inactivation of labile blood components was introduced in some developed countries in the not too distant future. This is despite the knowledge that in countries such as England, the current residual risk of HIV transmission by transfusion is of the order of 1 in 8 million units transfused; the risk of HCV transmission is 1 in 33 million and the corresponding risk for HBV transmission is 1 in 1 million. Whether we should continue introducing measures to continue decreasing the minute risk of transfusion-transmitted viral infections is not a matter to be decided in isolation by blood transfusion services, but by Governments, healthcare communities and the public at large.

A hypothetical risk of transfusion, unique to the UK, is the possibility of transmission of vCJD. This is due to the strong lymphoreticular association of the pathologic prion PrP^{sc} with lymphoid tissue, which is closely in contact with blood. The fear of transmissibility has increased since it was published that BSE (mad cow disease) could be transmitted experimentally by transfusion in sheep. The UK has spent considerable resources in trying to prevent this hypothetical risk. Fortunately, so far, no cases of transfusion–transmitted vCJD have been reported despite active surveillance. Altogether, up to September 2003, only 131 cases of vCJD have been reported in the UK, suggesting that the epidemic might not be of the magnitude predicted 2-3 years ago. Although several groups are actively trying to develop a screening test for vCJD in blood donations, no assay seems to be materializing in the near future.

The risks of over-transfusing patients are grossly underestimated. It is well known that some old patients with cardiac failure suffer significant morbidity and even mortality due to post-transfusion volume overload. It is also a fact that many patients are transfused perioperatively with the mere objective of keeping the Hb level at an "ideal" figure, with disregard to the patient's compensatory mechanisms; this is so much that some patients leave the hospital with a Hb level above their own normal level. On the other hand, there are those surgeons and anesthetists who are so keen on reducing allogeneic blood exposure and consequently reducing the Hb trigger below the "magical" figure of 10 that they undertransfuse their patients with the impending risk of silent myocardial infarction.

The interest in transfusion-transmitted infections has meant that Transfusion Medicine and Transfusion Services have developed significantly and great emphasis has been put on Quality, Audit and Good Manufacturing Practice (GMP). On the other hand, we realized that there were no surveillance systems in place for blood transfusion processes and activities. We were not aware of the real

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risks of transfusion nor of the magnitude of such risks. It is laudable that France instituted the first system of national haemovigilance. This well-organized, well-resourced, mandatory system was instituted in January 1994. Haemovigilance is defined as "the set of procedures of surveillance organized from the collection of blood and its components to the follow-up of its recipients with the purpose of collecting and evaluating information on the undesirable and unexpected effects resulting from the use of blood products and of preventing their occurrence".

SHOT (Serious Hazards of Transfusion), the UK voluntary, anonymous system of haemovigilance shortly followed, in November 1996. SHOT invites reports of major adverse events surrounding the transfusion of single or small pool blood components supplied by the UK National Blood Services (red cells, platelets, fresh frozen plasma, methylene blue FFP and cryoprecipitate). It does not cover complications due to fractionated plasma products. It is a confidential and atomized scheme of voluntary reporting. Hospitals report events under the following categories:

- Incorrect blood component transfused, (IBCT) regardless of harm to recipients.
- Acute transfusion reaction (within 24 hours).
- Delayed transfusion reaction (beyond 24 hours).
- Transfusion-associated graft-versus-host-disease (TA-GVHD).
- Transfusion-related acute lung injury (TRALI).
- Post-transfusion purpura (PTP).
- Transfusion transmitted infection (TTI) comprising.
- Bacterial contamination.
- Post transfusion viral infection.
- Other post-transfusion infection e.g. malaria.
- "Near Miss" events.

At hospital level, hazards are reported to the local hematologist. Suspected transfusion-transmitted infections must be reported to the supplying blood center to ensure prompt withdrawal of other implicated components and appropriate follow-up of donors and other possible recipients. Blood Center personnel are then responsible for onward reporting to the Communicable Disease Surveillance Center (CDSC) of the Public Health Laboratories (PHLS). Non-infectious hazards may be reported directly to the SHOT office using a simple "initial report" form. This is followed-up by a detailed specific questionnaire. Once complete, anonymized data is entered using a unique identification number and the paper records are shredded to prevent trace-back to individual cases. Collection and analysis of data on infectious hazards commenced in 1995, preceding that on non-infectious hazards by one year.

From 1996-2001, the SHOT scheme has collected a powerful body of data on serious transfusion complications in the UK from which to make firm recommendations for improvements in transfusion safety. The four UK Blood Services issue approximately 3.5 million blood components each year. Since 1996 there has been a year-on-year, increase in the number of reports with 413 eligible hospitals on the scheme. By the fifth year participation was running at 92%. The increase in total reports is almost solely the result of an increase in "incorrect blood component transfusion" incidents.

Of 1148 fully analyzed reports, 699 (61%) were "wrong blood" incidents. Of these, 161 were ABO incompatible transfusions leading to 11 deaths and 60 cases of major morbidity. Seventy three were RhD incompatible leading to potential RhD sensitization in 17 females of child-bearing potential.

Immune complications comprised 35.7 % of reports with 70 cases of possible transfusion-related acute lung injury (TRALI), leading to 8 deaths definitely or probably related to transfusion, and a further 12 deaths possibly, making TRALI the second largest cause of transfusion-related mortality and morbidity after ABO incompatibility.

Transfusion-transmitted infection (TTI) comprised less than 3% of reports. From 1995 – 2001 there were 39 confirmed TTIs of which the majority (25 cases) were bacterial contaminations (21 platelets and 4 red cells), resulting in severe morbidity in most cases and 6 deaths.

The SHOT data closely demonstrates that, in high-resource countries, microbiological, and especially virological safety of the blood supply is advanced. Efforts should now be concentrated in preventing bacterial contamination and in other areas of Transfusion Medicine such as the encouragement of appropriate use of blood, safe administration of blood components, accurate patient and sample identification etc. Hemovigilance is a system that is simple and relatively inexpensive to institute and which should be implemented in all countries to inform health services about the real risks of transfusion and to improve transfusion safety and Transfusion Medicine practice.