ARTICLE

For the very first time since its inception, the UK Serious Hazards of Transfusion scheme failed to document a single case of bacterial transmission by blood transfusion during a recent 12-month period. Although clearly this is a milestone in transfusion science, John Barbara sounds a note of caution in his overview of the current situation.

Combating bacterial infections transmitted by transfusion

For many years the transmission of bacterial infection almost became accepted as one of the occasional (and sometimes fatal) complications of blood transfusion. With the recognition of the potential for transmitting viral infections by transfusion, the steadily increasing number of interventions to prevent such infections (all increasingly costly) has resulted in the virtual elimination of hepatitis B virus (HBV), human immunodeficiency virus (HIV) and hepatitis C virus (HCV) as transfusion risks in the developed world.

With the introduction of nucleic acid testing (one of the more expensive interventions), the residual transmission risk per donation has fallen to one in hundreds of thousands, or even millions. In the UK, the avoidance of transfusion risks from variant Creutzfeldt-Jakob disease (vCJD) costs the blood services well over £100 million per annum. So far, only three cases of probable prion transmission by blood transfusion have been documented.

> 'In the last decade, between three and six bacterial transmissions have been reported each year'

In contrast, in the last decade, between three and six bacterial transmissions (nearly a third of which prove fatal to recipients) have been reported each year. The UK reports of microbial transmissions collated by the Serious Hazards of Transfusion (SHOT) scheme are summarised in Table 1 (see page 1040 for a summary of the latest SHOT report). The number of reported microbial transmissions is listed for each year with the total (and percentage of total reported adverse events that are microbial) shown at the bottom. Similarly, the number (and percentage) of microbial transmissions that are bacterial (and the percentage of these that are fatal) are indicated.

Not surprisingly, the majority of cases of bacterial transmission result from platelet transfusions, as they are stored at 22°C. The longer a platelet preparation is stored, the

Table 1. Serious Hazards of Transfusion reports (UK), October 1996 to December 2004 (source SHOT).

REPORT YEAR	ALL REPORTED ADVERSE EVENTS	MICROBIAL (%)	BACTERIAL	BACTERIAL AS % OF MICROBIAL	FATAL BACTERIAL	% OF BACTERIAL FATAL
1996/97	169	8	3	38	0	0
1997/98	196	3	1	33	1	100
1998/99	255	9	6	67	2	33
1999/00	293	6	5	83	2	40
2000/01	315	6	4	67	1	25
2001/02	(363) 478 (15m)	5	5	100	0	0
2002/03	480	8	3	38	1	33
2003/04	53.9	1	0	0	0	0
Totals	2725	46 (1.7)	27	59	7	26

greater the chance of a bacterial transmission. The contaminating bacteria are usually skin commensals introduced to the blood unit during venepuncture (ie an exogenous source). In contrast, the much more rare bacterial transmissions via red cell transfusions are due mainly to endogenous bacteria present in the blood donation because of an asymptomatic or subacute infection in the donor.

Typically, these involve organisms such as *Yersinia enterocolitica*, a psychrophilic bacterium than can replicate slowly at 4˚C (the storage temperature of red cell preparations) so that when transmission occurs the red cell units tend to be near the end of their shelf life. The transmissions of pseudomonads (also psychrophilic) reported in the past due to exogenous contamination are now avoided because of improved procedures for the preparation of blood components.

What is the current situation?

As shown in Table 1, 2003–04 was the first year in which no bacterial transmissions by transfusion were reported to SHOT. Subsequently, possible transfusion transmissions continue to be investigated exhaustively. Although it would be premature to conclude that we now have a complete grip on bacterial complications of transfusion, 2003–04 was a milestone year in this respect.

How did this occur?

Considerable research and development efforts around the world (including those at the National Blood Service's National Transfusion Bacteriology Laboratory [NTBL] led by Carl McDonald) identified a range of interventions with the potential to reduce the bacterial hazards of blood transfusion. These included:

- enhancing the efficacy of the disinfection or cleansing of the venepuncture site on the donor's arm
- diversion of the first 20–30 mL of a blood donation into a side pouch (which can provide the samples for subsequent routine laboratory screening), thus 'flushing' the exogenous skin contaminants away from the actual blood donation
- testing blood components (especially platelets) either prior to storage or prior to issue
- various combinations of the above
- microbial inactivation (pathogen reduction) of labile blood components.

'Research efforts around the world have identified interventions with the potential to reduce the bacterial hazards of blood transfusion'

Table 2. Expected effect of interventions on frequency of bacteria in platelets.

INTERVENTION	EXPECTED REDUCTION (%)	CONFIRMED?
Diversion	52	Yes
Disinfection	57	Yes
Divert and disinfect	71	Yes
Testing	80	No
Divert, disinfect and test	94	No
Inactivate	100	No

It is beyond the scope of this article to describe the many detailed aspects of these interventions and the investigations undertaken. Table 2 summarises the predicted efficacy of such interventions and the outcome of investigations undertaken at NTBL to examine actual outcomes. Similar work in other laboratories internationally provides broad corroboration.

The 71% reduction in the frequency of bacterially contaminated platelets following the use of diversion and enhanced donor arm disinfection was assessed following extensive prospective investigations, and efficacy seems to be borne out in the current reduction in cases of bacterial transmissions by transfusion reported to SHOT. As an additional safety measure, several blood services in other countries test platelet preparations for the presence of bacteria. Although under consideration and investigation by the NBS, no decision on such testing has yet been reached.

Several issues need to be considered with regard to testing. These include the type of test, when to test, whether or not anaerobic detection is required, how long to incubate, the volume of sample for testing, the sensitivity of the assay, and whether or not the platelet shelf life can be extended.

The future

Improving the disinfection of donors' arms (largely by using systems to help ensure that cleansing procedures are performed correctly) and the introduction of diversion pouches appears to have had a major impact in reducing the risk of bacterial transmission by transfusion. This situation can be confirmed and further quantified only by continued thorough reporting, investigation and collation of cases via SHOT, with subsequent monitoring and assessment by blood services.

The option for bacterial testing of platelets remains, and an increasing number of manufacturers now produce a wide range of assay systems – often of considerable ingenuity – or methods that detect organisms directly to complement bacterial culture methods. For example, microbial inactivation (eg with the psoralen amotosalen HCl [Cerus Laboratories]) has been shown to be very effective against a wide range of bacteria. However, because it is costly, somewhat cumbersome and thus far has only been available for platelet preparations, it has not been adopted widely.

The ultimate yardstick for the 'bacterial safety' of blood transfusion may be the comparison with 'viral safety' in relation to cost and benefit. If the residual risk of microbial transmission per donation is one in a million or less (actuarially considered as negligible), is it appropriate to aim for even greater safety? This question is particularly pertinent when compared to other healthcare risks, but the issue is confounded by European Product Liability (consumer protection) laws, which define blood as a 'product' and thus in effect demand 'zero risk'.

So, this story is set to continue! ■

I am grateful to Carl McDonald and Kate Soldan upon whose bacterial and epidemiological expertise I have drawn extensively.

USEFUL READING

- Blajchman MA, Beckers EA, Dickmeiss E *et al*. Bacterial detection in platelets: current problems and possible resolutions. *Transfus Med Rev* 2005; **19**: 259–72.
- Lin L. Photochemical inactivation of viruses and bacteria in platelet concentrates by use of a novel psoralen and long wavelength ultraviolet light. *Transfusion* 1997; **37**: 423–35.
- McDonald CP, Lowe P, Robbins S *et al*. Evaluation of donor arm disinfection techniques. *Vox Sang* 2001; **86**: 178–82.
- Stainsby D, Cohen H, Jones H *et al*. Serious Hazards of Transfusion (SHOT). SHOT Annual Report, 2003 (see also subsequent SHOT reports).

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