18. TRANSFUSION-TRANSMITTED INFECTIONS

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

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

and, either

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

or

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

Introduction

Infectious complications following transfusion differ from non-infectious complications in several ways that may affect the ascertainment and investigation of incidents. The onset of symptoms related to a transfusion-transmitted viral infection may occur from several weeks to years after the date of the transfusion. Reports of infections transmitted by transfusion in a particular year can therefore accrue over the subsequent year(s). The number of cases ascertained by the end of any period is therefore expected to be an incomplete picture of the infections transmitted during that period. 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 TTI 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.

PTIs 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 NBA and the PHLS CDSC in October 1995. Reported data from England, Wales and Northern Ireland are included in this report.

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

Methods

Participating blood centres in England Wales and Northern Ireland reported all PTIs of which they had been informed to the NBA/PHLS CDSC infection surveillance system. The criteria for identifying infections eligible for reporting as PTIs 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).

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

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

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

Data received by 31/12/2001 about incidents of TTIs initially reported by blood centres between 01/10/2000 and 30/09/2001 were included in this report. Data received about incidents reported during the previous five 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 PTIs were classified as PTIs of undetermined source.

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

Results

Blood centres in England, Wales and Northern Ireland made 38 initial reports of PTIs during the report year. An additional 9 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 PTI as stated above, but may have been reactions of bacterial origin). For three of these 9 reports another cause of the reaction was subsequently confirmed: 1 hypertension, 1 ATR (included in chapter 13), 1 TRALI (included in chapter 15). Reports were received from 8 of the 12 blood centres in England, Wales and Northern Ireland. These 8 centres collect approximately 70% of the donations tested each year in England, Wales and Northern Ireland. Two (5%) PTIs (1 bacteraemia, 1 HCV infection) were classified as PTIs of undetermined source due to inconclusive investigation of the donation(s) implicated as the source of infection. For 21 (55%) PTI reports (8 bacteraemia, 4 HBV infections, 6 HCV infections, 3 HIV infections), 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 (HBVx2: surgery & liver transplant, HCVx2: occupational contact with blood, HCV x1: travel in India, HIV x1: lived in sub-Saharan Africa).

Blood centres in Scotland reported five PTI investigations during the report year. Three post-transfusion HBV infections and 1 post-transfusion HCV infection were found to be not due to transfusion (one HBV with other source [health care worker] identified). One post-transfusion HBV infection reported during this year (transfused in 1997) is still under investigation. Scottish cases reported since October 1998 are included in the numbers of PTIs and TTIs shown in the tables and figures in this report. (In previous years these cases have not been included in the tables/figures.)

Figure 22 shows the classification of reports during the report year.

Of the 43 PTIs initially reported by blood centres in the UK between 01/10/2000 and 30/09/2001, 6 (14%) were classified, after appropriate investigation, as TTIs. Table 40 shows the TTIs reported between 01/10/2000 and 30/09/2001 by year of transfusion: 4 (3 bacterial contaminations and 1 HBV) were transfused during the report year, and 2 were transfused prior to the report year.

Figure 22
Classification of post-transfusion infections (and post-transfusion reactions) initially reported between 01/10/2000 and 30/09/2001.

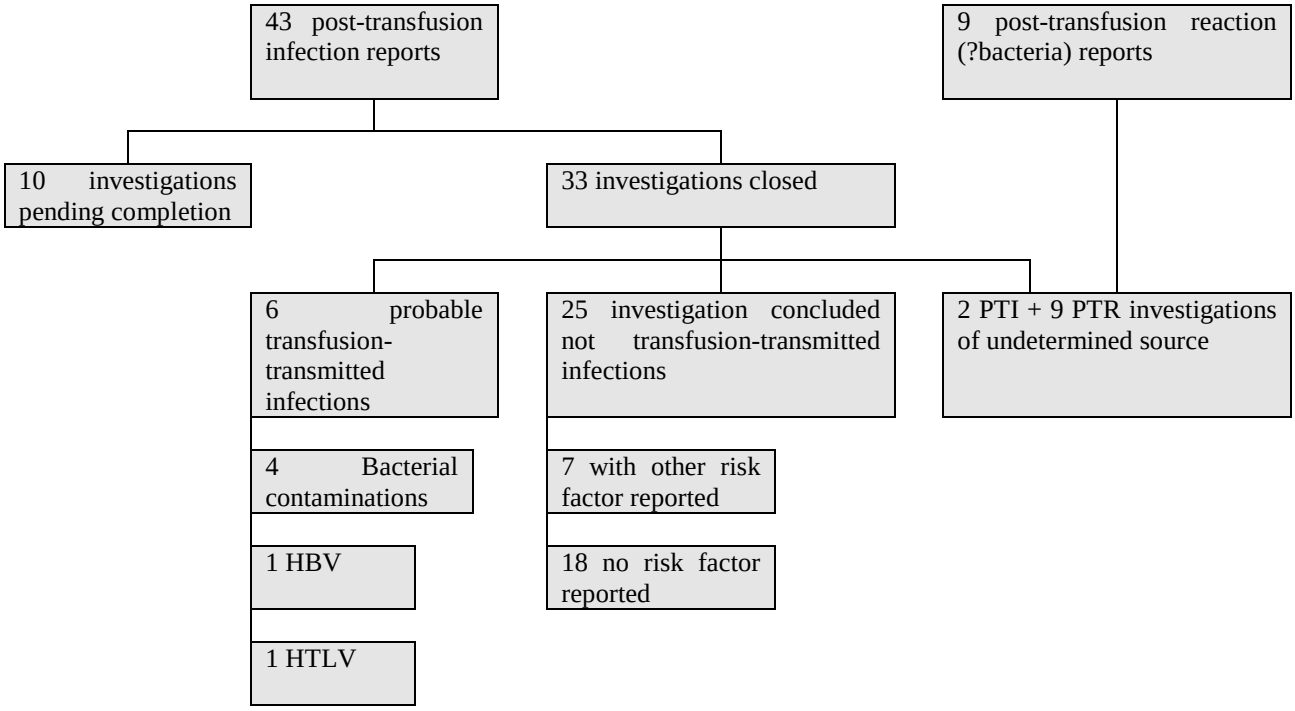


Table 40
TTIs reported between 01/10/2000-30/09/2001 by year of transfusion. The number of incidents is shown, with the total number of identified infected recipients shown in brackets.

Year of transfusion	Pre-2000	2000	2001 (to end Sept)	Total[b]
Infection				
HBV	-	1(1)	-	1(1)
HTLV	1(1)	-	-	1(1)
Bacteria	-	3(3)[a]	1(1)	4(4)[a]
Total	1(1)	4(4)[a]	1(1)	6(6)[a]

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

Details of TTIs

A. Infections for which donation testing is mandatory

Hepatitis B virus
One transfusion transmitted HBV infection was reported during this year. One recipient (50 year old male) was found by routine testing during dialysis treatment to be HBsAg positive and HBV DNA positive 4 months after transfusion to treat anaemia (associated with kidney disease). This recipient, who was immunosuppressed, had not developed any antibodies to HBV by 5 months after the implicated transfusion. The archive sample for 1 unit of red cells transfused to this recipient that had been found to be HBsAg negative at the time of donation was found to be HBsAg positive on re-testing with a different assay and was also found to be HBV DNA positive and anti-HBc negative. Subsequent testing of several samples from the donor indicated that he had suffered a recent HBV

infection and was now immune (HBsAg negative, anti-HBc positive, anti-HBs increasing to >500 iu/L by 7 months post-donation). This donor did not have any risk factors that should – according to guidelines in place at the time - have excluded him from donating blood. The probable source of the recipient's HBV infection was concluded to be an HBV DNA positive, anti-HBc negative, HBV infectious donation, with low level HBsAg, collected from a donor with early acute HBV infection.

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

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

B. Infections for which donation testing is not mandatory

Bacterial contamination
Four transfusion-transmitted bacterial contaminations were reported.

One recipient (60 year old female) developed fever during transfusion with a 5-day old unit of apheresis platelets during treatment for leukaemia. *Staphylococcus epidermidis* of an identical strain was cultured from the recipient's blood and the platelet pack. The probable source of the recipient's reaction was concluded to be a unit of apheresis platelets contaminated with *Staphylococcus epidermidis*: no source of this contamination was identified.

One recipient (40 year old male) developed fever, rigors and chest tightness after transfusion with a 5-day old unit of apheresis platelets during treatment for thrombocytopenia. *Staphylococcus aureus* with the same antibiotic sensitivities was cultured from the recipient's blood, the platelet pack and swabs from the donor's antecubital skin (there was no growth from nasal and throat swabs from the donor). The probable source of the recipient's reaction was concluded to be a unit of apheresis platelets contaminated with *Staphylococcus aureus* from the donor's arm.

One recipient (57 year old female) suffered a fatal reaction after transfusion with a 4-day old unit of pooled platelets during treatment for severe liver disease. *Bacillus cereus* was isolated from the implicated unit and from arm swabs of one of the four donors (the isolate from the arm swab was of a different strain). No organisms were found by culture of the four related red cell units. The probable source of the recipient's reaction, and death, was concluded to be a unit of pooled platelets contaminated with *Bacillus cereus* from a donor's arm.

One recipient (23 year old male) felt unwell with tightness around the throat and shivering, raised temperature and tachycardia several minutes after the start of transfusion with a 4-day old unit of pooled platelets during treatment for aplastic anaemia. This recipient was on antibiotics at the time and no bacteria were isolated from his blood cultures and he recovered within 2 days. Group B *streptococcus* was isolated from the implicated platelet unit. Culture of throat and arm swabs from the donors of this unit did not isolate any group B streptococcus. The probable source of the recipient's reaction was concluded to be a unit of pooled platelets contaminated with group B *streptococcus*: no source of this contamination was identified.

HTLV
One transfusion-transmitted HTLV-I infection was reported during this year.
One recipient (20 year old female) was traced and tested for HTLV-I infection after the donor of a component of red cells she had been given nine years previously (1991) presented as a patient with adult T-cell lymphoma (ATL) and was found to be infected with HTLV-I. This recipient, who received red cells during treatment for injuries from a road traffic accident, was the only recipient of six possibly infected components who was alive and fit to accept testing. This recipient was found to be positive for antibodies to HTLV-I, and to have weakly positive polymerase chain reaction results. She had had no symptoms of this infection. Neither the recipient nor the donor had any identified risk factors for HTLV-I infection. The probable source of the recipient's HTLV-I infection was concluded to be an HTLV infectious donation that entered the blood supply, in the absence of donation testing for HTLV, from a donor with no identifiable high risk for this infection.

Underreporting

The cases ascertained by this surveillance system were diagnosed, suspected to be attributable to transfusion, communicated to the blood service, and reported by a blood centre to the surveillance centre. At any one of these steps, other PTIs may have been missed and the extent of underreporting of PTIs is therefore unknown. The proportion of PTIs 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. 01/10/1999 to 30/09/2000) 5 TTIs were reported (see SHOT Annual Report 1999-00[9] for details of these cases).
One post-transfusion bacteraemia reported during the 1999-2000 year that was pending full investigation at the time of the last SHOT annual report has subsequently been concluded to be due to transfusion-transmitted bacteria. The recipient (58 year old male) suffered fatal septic shock after transfusion with a 2-day old unit of pooled platelets. *Staphylococcus epidermidis* (identical isolates) were cultured from the recipient and the implicated unit. Arm swabs of 3 of the donors were also culture positive for *Staphylococcus epidermidis* (but of different isolates). The probable source of the recipient's reaction and death was concluded to be a unit of pooled platelets contaminated with *Staphylococcus epidermidis* from a donor's arm.

The investigations of one post-transfusion HCV infection and one post-transfusion HBV infection (in Scotland) that were classified as pending full investigation in the 1999-2000 SHOT[9] report have subsequently been concluded to be not due to transfusion.
Table 41 shows the cumulative number of TTIs reported by the end of September 2001.

Cumulative data

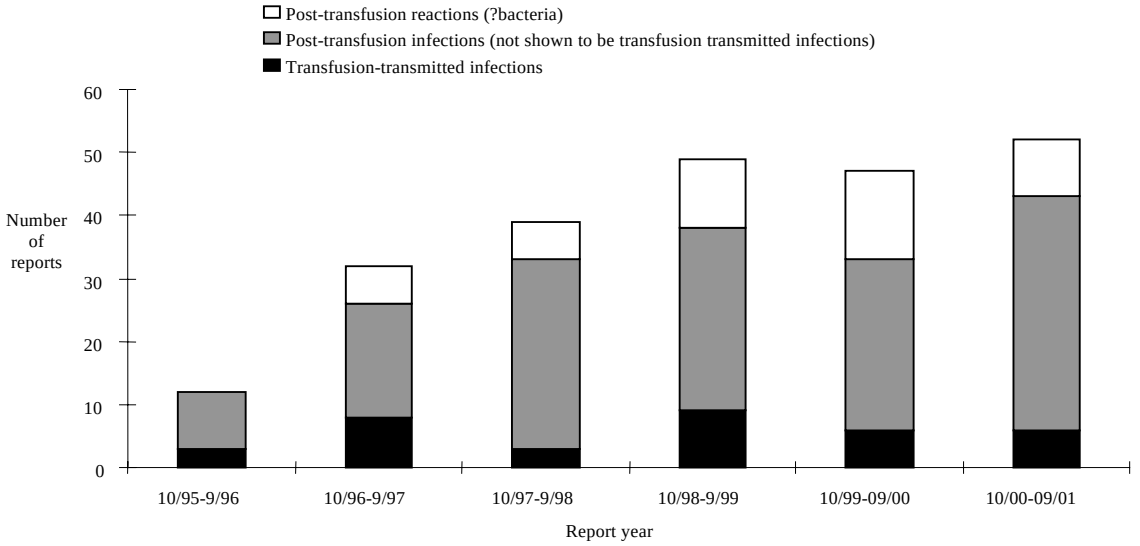
Figure 23 shows the cumulative number of reports received by year of transfusion since October 1995.

Table 41
Cumulative total TTIs: reported between 1/10/1995-30/09/2001 by date of transfusion. The number of incidents is shown with the total number of identified infected recipients in brackets.

Year of transfusion	Pre-1995	1995	1996	1997	1998	1999	2000	2001 (to end Sept)	Total	Deaths
Infection										
HAV	-	-	1(1)	-	-	-	-	-	1(1)	-
HBV	1(1)[b]	1(1)	1(1)	1(1)	1(1)	2(3)	1(1)	-	8(9)	-
HCV	-	-	1(1)	1(1)	-	-	-	-	2(2)	-
HIV[c]	-	-	1(3)	-	-	-	-	-	1(3)	-
Bacteria	-	1(1)	1(1)	3(3)	4(4)[ax2]	4(4)[a]	7(7)[ax3]	1(1)	21(21)	6
Malaria	-	-	-	1(1)[a]	-	-	-	-	1(1)	1
HTLV-I	1(1)	-	-	-	-	-	-	-	1(1)	-
Total	2(2)[b]	2(2)	5(7)	6(6)[a]	5(5)[ax2]	6(6)[a]	8(8)	1(1)	35(38)	7

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

Figure 23
PTI reports by report year (including Scotland from 10/98 onwards)



NB More reports are pending complete investigation in the most recent report year.

Cumulative data about bacterial contaminations

Table 42 shows a summary of the species of bacteria and the type and age of the implicated components for the 21 transfusion-transmitted bacterial contaminations reported between 01/10/1995 and 30/09/2001.

Table 42
Transfusion-transmitted bacterial contaminations reported in UK between 01/10/1995 and 30/09/2001 by species and component type and age (N=21).

	Platelets Age (in days) at use							Red cells
	1	2	3	4	5	NK	All	
All species	*0*	*1*	*2*	*6*	*4*	*4*	*17*	*4*
Bacillus cereus				3[a]		1	4	
Coagulase negative Staphylococci					1		1	1 (23 days)
Enterobacter aerogenes			1[a]				1	
Escherichia coli			1[a]			1	2	
group B Streptococcus				1		1	2	
Serratia liquifaciens								1
Staphylococcus aureus					1	1[a]	2	
Staphylococcus epidermidis		1[a]		2	2		5	1 (32 days)
Yersinia entercolitica								1[a] (33 days)

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

Six of the 17 contaminated platelet units were collected by apheresis from single donors, 11 were recovered from whole blood donations (each from a pooling of four donations). For 8 of these 21 cases the donors' arms were confirmed by subsequent testing to have been the probable source of the contamination. For some others, investigation of donors' arms was incomplete or inconclusive but the nature of the contaminating organism was suggestive of a skin contaminant that was most likely to have been introduced to the pack at the time of collection. For 2 cases, the donor's blood was concluded to have been the source of the contamination (i.e. endogenous bacteria, so contamination of the pack not preventable by skin cleansing or diversion).

Cumulative data about Hepatitis B virus transmissions

Seven of the 8 transfusion-transmitted HBV infections reported between 01/10/1995 and 30/09/2001 have been concluded to be probably due to infectious blood collected from donors undergoing acute HBV infection, with only one (reported in the first reporting year) due to infectious blood from a donor with later stage HBV infection. This is a change from the pattern observed in earlier collations of transfusion-transmitted HBV infection, for example only 3 of 14 transfusion-transmitted HBV infections reported to the PHLS from 1991 to 1997 were found to be due to donations from donors with acute infection, with the majority being due to donations from donors with chronic infection.[45] This change may have implications for the choice of strategies to further reduce the risk of transfusion-transmitted HBV infection.

COMMENTARY

- Reported TTIs are rare: only 6 confirmed cases were recognised in the UK during this 12-month period of reporting. Investigations of a further 37 cases of PTI were reported. The majority (76%) of the closed PTI investigations reported during this year have been shown not to be caused by transfusion. For two of the closed investigations the investigations were inconclusive.

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

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

- Fifty percent or more of bacterial contaminations are due to skin flora entering the pack at the time of collecting the donation.

- One case of transfusion-transmitted HBV infection was reported this year. The source of the implicated donation in this case – as in 6 of the 7 other cases reported since 01/10/1995 – was a donor with acute HBV infection.

- One case of transfusion-transmitted HTLV-I infection was reported this year. The infection was detected by lookback to the recipients of donations from a donor subsequently diagnosed with symptomatic HTLV-I infection. The identified infected recipient has not had symptoms. Transfusion-transmitted HTLV infection has been previously documented in the UK.[46] LD may have reduced the risk of HTLV transmission by transfusion since these cases were transfused.[47] SHOT is aware that HTLV testing is currently under consideration in the UK with possible tests undergoing evaluation for use for donation testing. This would further reduce the risk of HTLV infection.

- One TTI (*Bacillus cereus*) reported during this year resulted in the death of the recipient. One other investigation that was concluded during this year (reported during the previous year) also found that transfusion-transmitted bacteria (*Staphylococcus epidermidis*) resulted in the death of a recipient.

- Numbers of reported cases are small and fluctuations in reports are to be expected. Also, the reporting system is probably biased towards infections that cause rapid onset of acute disease. However, it should be noted that bacteria have accounted for the majority of reported transmissions by transfusion and the majority of known deaths due to TTIs, not only in this year's cases, but also in the cumulative data.

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

RECOMMENDATIONS

- **The cumulative and continuing predominance of bacteria as causing TTIs and infection-related deaths provides strong support for efforts to prevent bacterial contamination of blood components: these include promoting adherence to current BCSH guidelines[4] regarding the visual inspection of units for any irregular appearance immediately prior to transfusion (particularly platelets), as well as evaluating additional or revised strategies to prevent the contamination of donations. Two strategies in particular are currently under investigation and development for implementation: improvements in the disinfection of donors' arms and diversion of the first few mL of blood collected (most likely to contain skin flora) away from the primary pack that is sent for component production. Methods for testing platelets for bacterial contamination are also under consideration.**

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

- **It would be appropriate for blood services to review the residual risk of transfusion-transmitted HBV infection and assess whether additional donor screening for HBV would bring benefits in terms of blood safety.**