Taking the results for all 22 recipients of blood from BSE-exposed donors, five clinical cases and three sheep showing evidence of infection in the absence of clinical signs were identified, giving an overall transmission rate of 36%.

One recipient was culled for health reasons at 1444 days post transfusion, two were culled with suspected TSE clinical signs at 2480 and 2160 days post transfusion respectively, and the remaining clinically negative sheep were culled between 2239 and 3068 days post transfusion. With one exception, examination of the tissues by IHC did not find evidence of infection. The exception (D337) was culled at 3018 days post transfusion and showed positive PrP^{Sc} labelling in the brain, but with a pattern distinct from that observed in other BSE-infected sheep. The brain PrP^{Sc} distribution involving major white matter tracts and sparing the dorsal motor nucleus of the vagus was similar to that of Nor98 (or "atypical" sheep scrapie) and therefore unlikely to be transfusion-related. No other sheep in the present study showed evidence of being infected with atypical scrapie.

Out of the ten sheep that were infected intravenously with BSE as positive controls, eight developed clinical signs confirmed by IHC, with an average IP of 702 days (± 61 days standard deviation). The remaining two animals were culled at 2591 days post infection and, although not demonstrably clinically affected, IHC showed PrP^{Sc} deposition in the brains and lymphoid tissues of both animals. These two sheep were heterozygous (PL_{168}) for the PrP polymorphism P168L (see above), while the other eight were homozygous (PP_{168}).

The PrP^{Sc} profile obtained by IHC from BSE positive recipients was the same as that found in the orally inoculated donors and in the positive controls[16]. In addition, characteristic BSE glycoform patterns were obtained by Western blot analysis of PrP^{Sc} positive donor and recipient sheep (data not shown; see[9]), and inoculation of brain homogenates from infected donors and recipients into a panel of inbred mouse strains produced IPs and lesion profiles characteristic of BSE (data not shown). Taken together, these results confirm that the strain characteristics were not altered following transmission *via* blood.

2) Scrapie transfusion experiment

Four out of ten recipients of whole blood and four out of ten recipients of buffy coat from donors in the pre-clinical phase of scrapie infection developed clinical signs of scrapie, which were confirmed by positive IHC results. One sheep transfused with buffy coat from the single clinical donor was also clinically affected and IHC positive (see Table 2 & Figure 2). Four of these cases (F144, F153, F141 & F143) were reported previously[9]. There were four intercurrent deaths at 354, 753, 1237 and 1615 days post transfusion respectively, and the eight remaining recipients were culled between 2329 and 2484 days post transfusion. These twelve animals were clinically negative at the time of death, and showed no detectable PrP^{Sc} by IHC. Thus, nine out of 21 recipients of blood from scrapie-exposed sheep developed clinical scrapie, giving an overall transmission rate of 43%.

The majority of confirmed scrapie cases in recipients (n = 7) occurred in the groups that received transfusions from donors in the late pre-clinical (>50% of estimated IP) or clinical phase of infection. Only 2 out of 9 recipients in these groups remained free

of infection. The other two positive recipients were in the group of 6 sheep that received transfusions from donors at 28-37% of estimated IP, and their IPs were much longer than the rest (1101 and 1138 days post transfusion compared to a range of 575-853 days in recipients of blood from donors at >50% of estimated IP). No disease was confirmed in the 6 recipients that received blood from donors at ≤20% of estimated IP.

The PrP^{Sc} profile obtained from brains of donors and recipients highlighted some differences in terms of presence of vascular plaques or glia-associated PrP^{Sc} in donors but not in recipients, or *vice versa* (unpublished data). Such discrepancies were interpreted as presence of more than one natural scrapie strain in the flock of origin.

Discussion

The outcome of the blood transfusion experiments showed that two different TSE agents, scrapie and BSE, could be efficiently transmitted between sheep by blood transfusion, using volumes similar to those employed in human transfusions. The overall transmission rates (percentage of all recipients that became infected) were 36% for BSE and 43% for scrapie. For BSE, the figure was much higher than anticipated because three of the eight BSE-infected recipients survived for long periods without showing clinical signs, whereas all the scrapie-infected recipients identified by IHC were also clinically positive. The greater probability of sub-clinical infection in recipients of blood from BSE-exposed donors is largely due to variability in the genetic susceptibility to infection among sheep used in the BSE experiment, which will be discussed below. The results are consistent with the known facts about transmission of vCJD by blood transfusion in humans[17]. Sixty-six individuals known to have received labile blood products from 18 donors who subsequently developed vCJD were followed up in an on-going study. Three of these recipients have been confirmed clinically and pathologically as vCJD cases, with intervals between transfusion and the development of clinical signs ranging from approximately 6½ years to 8½ years[18-20]. Another individual, who died of unrelated causes 5 years post transfusion, showed PrP^{Sc} deposits in lymphoid tissues but not brain at post mortem, and is thought to represent pre-clinical or sub-clinical infection[21]. These four individuals represent 6% of the total recipients, or 12.5% of recipients surviving longer than 5 years.

Various factors influence the transmission rate by transfusion in both sheep and humans, including: (i) the interval between blood donation and the onset of clinical signs in the donors, (ii) genetic variation in susceptibility of donors and recipients, and (iii) the blood component transfused.

1) Stage of incubation period of the donors at the time of blood donation.

The effect of the stage of incubation can best be deduced from the results of the scrapie transfusion experiment, since the PrP genotype of the sheep used (VRQ/VRQ) renders them almost 100% susceptible to natural and experimental infection[22]. The stage of incubation of the donor has a strong influence on the probability of transmission to the recipient (Figure 2). When donations were made at ≤20% of the estimated IP, there was no disease transmission, while donations made at >50% of the estimated IP produced an 80% transmission rate, with a mean IP of 729 days (SD ±

99) in the recipients. Blood collected at 28-37% of the estimated IP transmitted infection at a lower rate of approximately 33%, and with longer IPs in the recipients of >1000 days. The data are consistent with a gradual increase in infectivity in the blood, from approximately 30-50% of IP until the clinical phase.

In the BSE transfusion experiment, the correlation between stage of infection and transmission is not clear-cut, but shows the same general trend of increasing probability of transmission to recipients as infection progresses in the donors (Figure 2). Possible explanations for the lower transmission rates from pre-clinical BSE-infected blood donors compared to pre-clinical scrapie-infected donors include:

a) Variation in susceptibility to infection of both donor and recipient sheep. This will be discussed below.
b) Differences in the pathogenesis of natural scrapie and experimental BSE. VRQ/VRQ sheep naturally infected with scrapie have detectable PrP^{Sc} deposits in lymphoid tissues early after infection (i.e. <50% estimated IP)[23,24]. Time course studies of ARQ/ARQ sheep orally infected with BSE showed that PrP^{Sc} was not consistently detected in lymphoid tissues before at least 65% of the average IP[7]. If infectivity in blood correlates with its presence in lymphoid tissues, this could explain the differences observed in the two transfusion experiments.

The probability of transmission from pre-clinical donors is of greatest relevance to the human situation. In the case of the four transfusion-related transmissions of vCJD, the donors developed clinical signs between 17-42 months after donation. The mean IP for vCJD has been estimated to be 16.7 years, with a lower 95% confidence interval of approximately 12.4 years[25]. Therefore, it is likely that the transfusion-related vCJD cases resulted from donations made at least half-way through the IP, which is in agreement with the data from the sheep experiments. In vCJD cases, the timing of detectable lymphoid replication in the pre-clinical stages of disease is unknown; therefore it is not clear whether the peripheral pathogenesis more closely resembles BSE or natural scrapie in sheep.

2) Effect of genetic variation in susceptibility.

A small proportion of sheep with $A_{136}Q_{171}/A_{136}Q_{171}$ PrP genotypes do not succumb to infection following natural or experimental exposure to scrapie and BSE, or have very prolonged incubation periods[26-28]. The reasons for this variability in response are not clearly understood, but it can be predicted to reduce infection rates in both donor and recipient sheep in the BSE transfusion experiment. The majority of pre-clinical donor sheep (8/11) in the BSE transfusion experiment were killed at, or shortly after, the time of donation, and none showed conclusive evidence of infection, although two transmitted infection to their respective transfusion recipients. It is potentially significant that donors that failed to transmit infection were heterozygous at PrP codon 154, while those that did transmit infection were homozygous. Thus, variable susceptibility to infection among the donor sheep may be the result of a protective effect of codon 154 heterozygosity to oral challenge with BSE, although more data are required to confirm this association.

A novel polymorphism, resulting in a proline to leucine substitution at codon 168 of the PrP gene, was identified in four BSE transfusion recipients and two positive

control sheep inoculated intravenously with BSE[14]. All six survived >2000 days without developing clinical signs of BSE, but on post mortem examination four showed PrP^{Sc} deposition in brain and lymphoid tissues. This suggests that the P168L polymorphism can protect against clinical disease, but does not prevent infection by the intravenous route. This polymorphism has not been identified in the Edinburgh NPU Cheviots used as donors in the BSE experiment, nor in sheep with the VRQ/VRQ genotype.

Although the genetic basis of susceptibility to BSE infection in sheep and humans is not directly comparable, the variability in response to BSE found in ARQ/ARQ sheep provides a more realistic reflection of the situation with vCJD in the human population than the very uniform susceptibility of VRQ/VRQ sheep to scrapie infection. In addition, the survival of BSE-infected transfusion recipients for up to 7 years without clinical signs demonstrates that prolonged secondary incubation periods and/or a sub-clinical/"carrier" state are possible following transfusion in sheep. The existence of such sub-clinical or prolonged pre-clinical infection states in humans is recognised as one of the important factors influencing the probability of onward transmission, and thus the potential size of the vCJD epidemic[29]. Susceptibility to human TSEs has been linked to codon 129 of the PrP gene, which can encode either methionine (M) or valine (V). Until recently, all clinical cases of vCJD (including the 3 transfusion-related cases) that have been tested have been homozygous for methionine at 129 (129MM). Interestingly, the "pre-clinical" individual believed to have been infected by transfusion was heterozygous (129MV)[21]. There is accumulating evidence to suggest that all human 129 genotypes may be susceptible to vCJD infection, with apparently greater likelihood of sub-clinical infection in 129MV and 129VV individuals[30-32].

3) Effect of blood component.

The four transfusion-related vCJD infections occurred in individuals who received transfusions of red cells that had not been leucodepleted. Leucodepletion was introduced in the UK in 1999 to control the risk of transmission of vCJD by blood transfusion, because previous studies in rodents had shown that infectivity appeared to be concentrated in the buffy coat, which contains most of the blood leukocytes[4]. Subsequently, leucodepletion of blood from scrapie-infected hamsters was shown to remove up to 72% of infectivity[33,34]. In the sheep experiments, only whole blood and buffy coat were transfused, because we were seeking to establish proof of principle of transmission of TSEs by blood transfusion, and assessing whether infectivity appeared to be concentrated in the buffy coat. The effect of leucodepletion was not investigated, but is being addressed in a follow-up study, along with estimates of the distribution of infectivity among other blood components, including plasma, platelets and red cells.

In our experiments, transmission rates did not appear to be significantly different in recipients receiving whole blood compared to recipients transfused with buffy coat. The number of sheep transfused with buffy coat in the BSE experiment was too small to allow statistical analysis. In the scrapie experiment, five of the positive recipients were transfused with buffy coat, and four with whole blood. The similarity in transmission rates for both components suggests that they contain approximately equivalent amounts of infectivity.

We have shown that, for sheep infected with scrapie and BSE, high transmission rates can be achieved using blood transfusion, particularly when donors are at >50% of incubation period. The results also revealed the possibility of prolonged incubation periods and/or sub-clinical infections in some recipients of BSE-infected blood, which is at least partly due to genetic variation in the sheep PrP gene. The suggestion of relatively high titres of infectivity in blood is perhaps surprising in view of the need for ultra-sensitive methods of detection for PrP^{Sc} in blood[35,36]. It may be that, in blood, infectivity is not closely correlated with levels of protease-resistant PrP, but comparative titrations of brain and blood-borne infectivity in sheep will be required to further define the relationship. The results of our sheep transfusion experiments are consistent with what is known about transfusion-associated vCJD transmission in man, and support the use of sheep as an experimental model in which to study the risks associated with different blood products, the effectiveness of control measures and the development of diagnostic and screening tests.

Acknowledgements

This experiment was funded by the UK Department of Health (project reference 1216713). The BSE challenged donor sheep were part of an experiment funded by the Department of Environment, Food and Rural Affairs. We thank Calum McKenzie, Tony Smith, Richard Eynon, Emma Cartwright, Mhairi Baxter, Dr. Richard Lysons and colleagues for their excellent care of the sheep, and for technical assistance with blood collections/ transfusions, clinical scoring and post mortem tissue collection. We also thank Suzanne Beckett, Anne Coghill, Dawn Drummond, David Parnham, Aileen Boyle and Irene McConnell for pathology and mouse transmission work, and Paula Stewart for PrP genotyping. Technical contribution to IHC by Hazel Baird, Lynne Fairlie, Ann Dunachie and Maria Oliva is acknowledged. The Scottish National Blood Transfusion Service supplied the blood packs used for blood collection, and prepared the buffy coat fractions. We thank Professor C.J. Bostock for his advice and support for this project.

Author contributions

F.H. designed the study, performed transfusions and post-mortems on recipient sheep, analyzed data and wrote the paper. A.C. and S.McC. performed Western blots, and S.McC. reviewed the report. J.F. coordinated collection of blood and post-mortems on donor sheep. W.G. analyzed and interpreted PrP genotype data and reviewed the report. S.S. and L.G. examined tissues, interpreted IHC results, analyzed data and reviewed the report. M.J. contibuted to the interpretation of IHC results and reviewed the report. N.H. designed the study, analyzed data, and reviewed the report.

The authors have no financial conflicts of interest to declare.

References

1. Will RG, Ironside JW, Zeidler M, et al. A new variant of Creutzfeldt-Jakob disease in the UK. Lancet. 1996;347:921-925.
2. Hilton DA, Ghani AC, Conyers L, et al. Prevalence of lymphoreticular prion protein accumulation in UK tissue samples. J Pathol. 2004;203:733-739.

3. Hill AF, Butterworth RJ, Joiner S, et al. Investigation of variant Creutzfeldt-Jakob disease and other human prion diseases with tonsil biopsy samples. Lancet. 1999;353:183-189.
4. Brown P, Cervenakova L, McShane LM, Barber P, Rubenstein R, Drohan WN. Further studies of blood infectivity in an experimental model of transmissible spongiform encephalopathy, with an explanation of why blood components do not transmit Creutzfeldt-Jakob disease in humans. Transfusion. 1999;39:1169-1178.
5. Hadlow WJ, Kennedy RC, Race RE. Natural infection of Suffolk sheep with scrapie virus. J Infect Dis. 1982;146:657-664.
6. van Keulen LJ, Schreuder BE, Vromans ME, Langeveld JP, Smits MA. Pathogenesis of natural scrapie in sheep. Arch Virol Suppl. 2000;57-71.
7. Jeffrey M, Ryder S, Martin S, et al. Oral inoculation of sheep with the agent of bovine spongiform encephalopathy (BSE). 1. Onset and distribution of disease-specific PrP accumulation in brain and viscera. J Comp Pathol. 2001;124:280-289.
8. Houston F, Foster JD, Chong A, Hunter N, Bostock CJ. Transmission of BSE by blood transfusion in sheep. Lancet. 2000;356:999-1000.
9. Hunter N, Foster J, Chong A, et al. Transmission of prion diseases by blood transfusion. J Gen Virol. 2002;83:2897-2905.
10. Goldmann W, Baylis M, Chihota C, Stevenson E, Hunter N. Frequencies of PrP gene haplotypes in British sheep flocks and the implications for breeding programmes. J Appl Microbiol. 2005;98:1294-1302.
11. Jeffrey M, Martin S, González L, et al. Immunohistochemical features of PrP(d) accumulation in natural and experimental goat transmissible spongiform encephalopathies. J Comp Pathol. 2006;134:171-181.
12. González L, Martin S, Houston FE, et al. Phenotype of disease-associated PrP accumulation in the brain of bovine spongiform encephalopathy experimentally infected sheep. J Gen Virol. 2005;86:827-838.
13. González L, Martin S, Begara-McGorum I, et al. Effects of agent strain and host genotype on PrP accumulation in the brain of sheep naturally and experimentally affected with scrapie. J Comp Pathol. 2002;126:17-29.
14. Goldmann W, Houston F, Stewart P, Perucchini M, Foster J, Hunter N. Ovine prion protein variant A(136)R(154)L(168)Q(171) increases resistance to experimental challenge with bovine spongiform encephalopathy agent. J Gen Virol. 2006;87:3741-3745.
15. Kirby L, Goldmann W, Houston F, Gill AC, Manson JC. A novel, resistance-linked ovine PrP variant and its equivalent mouse variant modulate the in vitro cell-free conversion of rPrP to PrP(res). J Gen Virol. 2006;87:3747-3751.
16. Sisó S, González L, Houston F, Hunter N, Martin S, Jeffrey M. The neuropathologic phenotype of experimental ovine BSE is maintained after blood transfusion. Blood. 2006;108:745-748.
17. Hewitt PE, Llewelyn CA, Mackenzie J, Will RG. Creutzfeldt-Jakob disease and blood transfusion: results of the UK Transfusion Medicine Epidemiological Review study. Vox Sang. 2006;91:221-230.
18. Llewelyn CA, Hewitt PE, Knight RS, et al. Possible transmission of variant Creutzfeldt-Jakob disease by blood transfusion. Lancet. 2004;363:417-421.
19. Wroe SJ, Pal S, Siddique D, et al. Clinical presentation and pre-mortem diagnosis of variant Creutzfeldt-Jakob disease associated with blood transfusion: a case report. Lancet. 2006;368:2061-2067.

20. HPA. 4th case of variant CJD infection associated with blood transfusion. Health Protection Agency. 2007. http://www.hpa.org.uk/hpa/news/articles/press_releases/2007/070118_vCJD.htm
21. Peden AH, Head MW, Ritchie DL, Bell JE, Ironside JW. Preclinical vCJD after blood transfusion in a PRNP codon 129 heterozygous patient. Lancet. 2004;364:527-529.
22. Houston EF, Halliday SI, Jeffrey M, Goldmann W, Hunter N. New Zealand sheep with scrapie-susceptible PrP genotypes succumb to experimental challenge with a sheep-passaged scrapie isolate (SSBP/1). J Gen Virol. 2002;83:1247-1250.
23. Schreuder BE, van Keulen LJ, Vromans ME, Langeveld JP, Smits MA. Tonsillar biopsy and PrPSc detection in the preclinical diagnosis of scrapie. Vet Rec. 1998;142:564-568.
24. Andréoletti O, Berthon P, Marc D, et al. Early accumulation of PrP(Sc) in gut-associated lymphoid and nervous tissues of susceptible sheep from a Romanov flock with natural scrapie. J Gen Virol. 2000;81:3115-3126.
25. Valleron A-J, Boelle P-Y, Will R, Cesbron J-Y. Estimation of Epidemic Size and Incubation Time Based on Age Characteristics of vCJD in the United Kingdom. Science. 2001;294:1726-1728.
26. Goldmann W, Hunter N, Smith G, Foster J, Hope J. PrP genotype and agent effects in scrapie: change in allelic interaction with different isolates of agent in sheep, a natural host of scrapie. J Gen Virol. 1994;75:989-995.
27. O'Rourke KI, Holyoak GR, Clark WW, et al. PrP genotypes and experimental scrapie in orally inoculated Suffolk sheep in the United States. J Gen Virol. 1997;78:975-978.
28. Jeffrey M, Martin S, Thomson JR, Dingwall WS, Begara-McGorum I, González L. Onset and distribution of tissue prp accumulation in scrapie-affected suffolk sheep as demonstrated by sequential necropsies and tonsillar biopsies. J Comp Pathol. 2001;125:48-57.
29. Clarke P, Will RG, Ghani AC. Is there the potential for an epidemic of variant Creutzfeldt-Jakob disease via blood transfusion in the UK? J R Soc Interface. 2007;4:675-684.
30. Bishop MT, Hart P, Aitchison L, et al. Predicting susceptibility and incubation time of human-to-human transmission of vCJD. Lancet Neurol. 2006;5:393-398.
31. Ironside JW, Bishop MT, Connolly K, et al. Variant Creutzfeldt-Jakob disease: prion protein genotype analysis of positive appendix tissue samples from a retrospective prevalence study. Bmj. 2006;332:1186-1188.
32. Mead S, Joiner S, Desbruslais M, et al. Creutzfeldt-Jakob Disease, Prion Protein Gene Codon 129VV, and a Novel PrPSc Type in a Young British Woman. Arch Neurol. 2007;64:1780-1784.
33. Gregori L, McCombie N, Palmer D, et al. Effectiveness of leucoreduction for removal of infectivity of transmissible spongiform encephalopathies from blood. The Lancet. 2004;364:529-531.
34. Gregori L, Gurgel PV, Lathrop JT, et al. Reduction in infectivity of endogenous transmissible spongiform encephalopathies present in blood by adsorption to selective affinity resins. Lancet. 2006;368:2226-2230.
35. Castilla J, Saá P, Soto C. Detection of prions in blood. Nat Med. 2005;11:982-985.
36. Saá P, Castilla J, Soto C. Presymptomatic Detection of Prions in Blood. Science. 2006;313:92-94.

Figure 1. Overview of experimental design.

Figure 2. Outcome of transfusions as a function of the stage of disease incubation in the donor. A. BSE-infected donors. B. Scrapie-infected donors. For each stage of infection in the donor sheep, the number of uninfected (open bars), clinically positive/ IHC positive (solid bars) and clinically negative/IHC positive (cross-hatched bars) recipients are shown.

Table 1. Outcome of transfusions from BSE-exposed donor sheep.

Donor sheep details								Recipient sheep details				
Donor sheep ID	Donor genotype	Clinical status at donation	% actual or average incubation period at donation[a]	Clinical outcome	IHC result	Incubation period (days)	Component transfused	Recipient sheep ID	Recipient PrP 168 codon genotype	Clinical outcome	IHC result	Incubation period (days)
58x51	ARQ/ARQ	Preclinical	12	+	+	2131	WB	D529	PP	+[c]	-	-
60x49	ARQ/ARQ	Preclinical	22	-	+/- (DRG)[b]	-	WB	D433	PL	-	-	-
			44				WB	F14	PL	-	-	-
J2747	ARQ/AHQ	Preclinical	42	-	-	-	BC	F182	PP	-	-	-
			44				WB	F181	PP	-	-	-
61x24	ARQ/AHQ	Preclinical	42	-	-	-	BC	F238	PP	+[c]	-	-
		Preclinical	43				WB	F234	PP	-	-	-
J2746	AHQ/AHQ	Preclinical	45	-	-	-	WB	F19	PP	+	+	536
J2559	AHQ/AHQ	Preclinical	51	+	+	629	WB	D505	PP	+	+	610
58x81	ARQ/AHQ	Preclinical	61	-	+/- (IPP)[b]	-	BC	D358	PP	-	-	-
58x28	ARQ/AHQ	Preclinical	61	-	-	-	WB	D421	PP	-	-	-
			61				BC	D384	PP	-	-	-
58x27	AHQ/AHQ	Preclinical	61	-	-	-	WB	D452	PP	-	+[d]	-
			61				BC	D318	PP	-	-	-
58x39	ARQ/AHQ	Preclinical	62	-	-	-	WB	D337	PP	-	+[c]	-
			62				WB	D386	PP	-	-	-
J2499	AHQ/AHQ	Preclinical	86	+	+	761	WB	D341	PP	-	-	-
J2771	AHQ/AHQ	Clinical	100	+	+	561	BC	G61	PL	-	+	-
J2770	AHQ/AHQ	Clinical	100	+	+	589	WB	G74	PP	+	+	594
60x69	AHQ/AHQ	Clinical	100	+	+	660	WB	G78	PP	+	+	556
							BC	G49	PP	+	+	531
D383	ARQ/ARQ	Clinical	100	+	+	671	WB	G92	PL	-	+	-

Key: WB = whole blood, BC = buffy coat, DRG = dorsal root ganglion, IPP = ileal Peyer's patch

[a] Calculated from the days post-infection at the time of donation, as a percentage either of the final incubation period (in sheep kept alive until the development of clinical signs), or of the average incubation period in orally-infected donors (640 days), excluding the out-lying incubation period of 2131 days for 58x51.

[b] These tissues were initially scored weakly positive by IHC, but the results were not reproducible in two laboratories and can therefore be considered as inconclusive.

[c] No evidence of infection was found on post mortem examination of tissues from these clinical suspects; therefore it is most likely they were clinically misdiagnosed.

[d] This sheep died of unrelated causes (i.e. without showing clinical signs of BSE) at 1139 days post transfusion, but was positive by IHC.

[a] This apparently healthy sheep was culled 3018 days post transfusion and found to be positive by IHC; however further analysis suggested this was a case of "atypical" scrapie, and therefore unlikely to be transfusion related (see text for details).

Table 2: Outcome of transfusions from scrapie-exposed donor sheep

Donor sheep details								Recipient sheep details			
Donor sheep ID	Donor genotype	Clinical status at donation	% actual or average incubation period at donation[a]	Clinical outcome	IHC result	Incubation period (days)	Component transfused	Recipient sheep ID	Clinical outcome	IHC result	Incubation period (days)
67x42	VRQ/VRQ	Preclinical	17	+	+	1274	BC	G247	-	-	-
			19				WB	G230	-	-	-
66x45	VRQ/VRQ	Preclinical	17	-	-	-	WB	G267	-	-	-
			19				BC	G265	-	-	-
67x23	VRQ/VRQ	Preclinical	18	+	+	1207	BC	G241	-	-	-
			20				WB	G228	-	-	-
65x13	VRQ/VRQ	Preclinical	28	+	+	1556	WB	F275	-	-	-
			30				BC	F273	-	-	-
65x02	VRQ/VRQ	Preclinical	34	-	+	-	WB	F310	-	-	-
			37				BC	F309	+	+	1101
65x03	VRQ/VRQ	Preclinical	34	-	+	-	WB	F277	+	+	1138
			37				BC	F276	+[b]	-	-
61x75	VRQ/ARQ	Preclinical	53	+	+	1324	BC	F149	+	+	782
			57				WB	F144	+	+	672
61x68	VRQ/VRQ	Preclinical	64	+	+	1113	BC	F152	+	+	853
			69				WB	F153	+	+	660
61x66	VRQ/VRQ	Preclinical	62	-	ND	-	WB	F286	-	-	-
			64				BC	F284	-	-	-
59x27	VRQ/VRQ	Preclinical	73	+	+	1137	BC	F126	+	+	826
			77				WB	F141	+	+	575
59x28	VRQ/VRQ	Clinical	100	+	+	1081	BC	F143	+	+	737

[a] Calculated from the age at the time of donation, as a percentage either of the final incubation period (for sheep that survived until the development of clinical signs), or of the average incubation period (1296 days) for sheep that died or were culled before developing clinical signs.

[b] No evidence of infection was found on post mortem examination of tissues from this clinical suspect; therefore it is most likely it was clinically misdiagnosed.