approximately 1000 times less sensitive than a similar assay in cattle (BSE Inquiry 2000b).

Lateral (close association) transmission of BSE – mouse and transgenic mouse models

The infectivity of the placenta was studied for its potential involvement in the lateral transmission of BSE from mother to offspring. Studies in sheep had shown that placental transmission is an endemic route of infection of lambs with scrapie (Brotherston and others 1968). However, feeding mice with milk, udder, supramammary lymph nodes, placenta and fetal membranes from BSE-infected cattle failed to transmit the disease (Middleton and Barlow 1993); again, these results were considered inconclusive owing to the effect of the species barrier between mice and cattle.

As a method for overcoming the species barrier, researchers created a prion 'knockout' mouse that had its endogenous prion gene disrupted or made inactive. The knockout mice did not make any prion proteins and did not become diseased when exposed to infective prions. The knockout mouse line was then made transgenic by adding the cattle prion gene to their genome, so that the mice would express cattle prions; BSE can be transmitted to these mice much more easily and with much shorter incubation times. These transgenic mice have provided a more sensitive bioassay by eliminating the species barrier and by more closely approximating the aetiology of the disease in cattle (Scott and others 1997).

In a transgenic mouse line expressing bovine prion protein (boTg), BSE prions were detected in the brains of pups born to mothers infected intracerebrally when they had been mated close to the clinical phase of the disease. However, the intracerebral inoculation of transgenic boTg mice with infected milk was ineffective, suggesting that mother to offspring transmission involved other tissues as carriers of infected prions (Castilla and others 2005a, b).

Table 1 gives a summary of various animal systems and knowledge of the transmission of BSE in milk (direct evidence), or from mother to offspring and lateral transmission (indirect evidence).

DISCUSSION

The transmission of BSE in milk has not been reported from any BSE-affected country and there is similarly no evidence of the transmission of scrapie or the human spongiform encephalopathies (CJD and kuru) in milk. The lack of evidence suggests that milk either does not readily transmit infective prions (Haltia and others 1979, van Duijn and others 1998, Vetrugno 2004), or that its infectivity is too low.

The risk of acquiring vCJD from drinking milk appears to be much lower than from eating other specified risk materials, beef or other tissues from BSE-infected cattle. Data to support the very low risk attributable to contaminated milk comes from the suckler herd study completed in the UK in 1997, which was designed specifically to investigate milk safety. Investigations with suckling cows under practical conditions provided no evidence that BSE was transmitted from the milk of infected cows to their calves (Wilesmith and others 1997).

In 1997, the Scientific Steering Committee of the European Commission categorised BSE risk materials into four categories. Colostrum, milk and mammary gland tissues were classified in category 4, as tissues in which infectivity could not be detected. At that time, the term 'not detected' did not mean 'not present' because the mouse bioassay system was insensitive to BSE infectivity. The classification indicated that there was no evidence that the tissues could propagate the disease.

In November 2003, at the request of the Chief Medical Officer for England, the Spongiform Encephalopathy Advisory Committee (SEAC) considered evidence on the potential transmission of vCJD from mother to child in utero and from breast milk. The committee had limited epidemiological and experimental research on the maternal transmission of prion diseases to work with. Using unpublished surveillance data on children born to vCJD mothers from the National CJD Surveillance Unit and the surveillance of progressive intellectual and neurological deterioration of neurological illness in children in the UK (Devereux and others 2004), the committee concluded that there was no epidemiological evidence for the maternal transmission of vCJD, including transmission by breast milk, but acknowledged that there was a hypothetical risk. The evidence was limited and mostly indirect but the risk appeared to be low for this high-risk group. The government position remains that infected milk should be banned from human consumption (SEAC 2004). Research in the UK, funded by the Department for Environment, Food and Rural Affairs and the Food Standards Agency concerning the safety of milk and the transmission of prions is continuing.

Despite the low risk determined from several research studies, one study pointed out the possibility of passing prions in milk. A Japanese woman dying of CJD was found to have the infectious prions in her colostrum (Tamai and others 1992). However, this result was later retracted because the Japanese research authorities that repeated the work found that lateral transmission could not be discounted as the route of exposure, and the results of the infectivity in milk were not repeatable. The secondary contamination of milk can virtually be excluded because milk from animals in commercial dairy operations is unlikely to contain colostrum (Vetrugno 2004).

Perhaps the most compelling evidence that milk constitutes a negligible risk comes from work by Everest and others (2006), who found that no abnormal prion proteins were detectable in the cell fraction of milk from cattle incubating BSE either by a modified commercial BSE ELISA or a second confirmatory assay.

Although clinically healthy animals do not appear to transmit prions, recent work by Ligios and others (2005) and Aguzzi (2006) suggests that inflammation in the secretory organs and the coexistence of a prion infection may lead to the contamination of secretions by prions. Concurrent diseases such as a viral infection of the mammary gland and inflammation may induce conditions in which prions are secreted in milk. Although the available evidence is limited, the health risk to human beings as a result of consuming milk or milk products from BSE-infected cows appears to be negligible.

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別紙様式第 2-1

別紙 3-5

医薬品
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識別番号・報告回数		回	報告日 年　月　日	第一報入手日 2006 年 12 月 8 日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称			研究報告の公表状況	Creutzfeldt-Jakob disease and blood transfusion: results of the UK transfu- sion medicine epidemiological review study. Hewitt, P.E. et al. Vox sanguinis, 91, 221-230 (2006)	公表国 英国	
販売名（企業名）						

研究報告の概要	使用上の注意記載状況・その他参考事項等
この論文では，英国で実施中の大規模研究における 2006 年 3 月までの結果が報告された。本研究の目的は散発性 (sCJD)，家族性 (fCJD)，変異型クロイツフェルト・ヤコブ病 (vCJD) の輸血を介して伝播した証拠となるものがあるかどうかを明らかにすることである。vCJD18 例，sCJD3 例及び fCJD3 例の血液成分はそれぞれ 66，20，11 名の患者に輸血されたことが確認された。今日現在，vCJD 感染は 3 症例のみ確認されている。2 名の vCJD 感染者はそれぞれ白血球非除去赤血球製剤を輸血された 6.5 年 (R1)，7.8 年 (R2) 後に発症した。これらのドナーは献血後 40 ヵ月目と 21 ヵ月目にそれぞれ臨床症状を示していた。2 名の輸血受容者のプリオンタンパク遺伝子の 129 番目のコドンはホモ接合体のメチオニンであり，vCJD に感染しやすいことが確認されている。R1 は認知症と癌の併発で死亡 (後に vCJD と確認された)，その一方で R2 は「vCJD の可能性あり」と診断されたが 2006 年 3 月現在生存している。3 症例目 (R3) は献血の 18 カ月後に臨床症状を発症したドナーから赤血球の輸血を受けていた。R3 は輸血の 5 年後に CJD と無関係の原因で死亡，その 129 番目のコドンはヘテロ接合体であった。しかし，剖検の際，プロテアーゼ耐性の異常型 PrP^{res} タンパクは，脾臓とリンパ節の一部で検出されたが，脳からは検出されなかった。そのため，この症例は発症前または無症候感染であったと考えられる。一方，fCJD 及び sCJD の輸血感染報告はなかったが，fCJD 及び sCJD 感染ドナーの症例数が少ないことを考慮すると，結論付けられる結果ではない。結論として，この継続中の研究において，おそらく過小評価していた輸血を介したヒト間での vCJD 感染リスクが存在することが明らかになった。	BYL-2007-0263

報告企業の意見	今後の対応
英国で実施されたこの大規模な調査は，sCJD および fCJD については結論が出されていないが，既に懸念されている輸血を介した vCJD 感染の可能性については確認できたと考えられる。しかしながら，弊社の血漿分画製剤，コージネイト FS あるいはコージネイト FS バイオセット注の製造工程で使用されている血漿分画製剤は，米国で採集されているため，vCJD リスクは非常に小さいと考えられる。さらに，これら血漿分画製剤の製造工程では，非常に効果的であることが実験上確認されているプリオン除去工程が組み込まれている。	現時点で新たな安全対策上の措置を講じる必要はないと考える。

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ORIGINAL PAPER

Creutzfeldt–Jakob disease and blood transfusion: results of the UK Transfusion Medicine Epidemiological Review study

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Vox Sanguinis

Background and Objectives This paper reports the results to 1 March 2006 of an ongoing UK study, the Transfusion Medicine Epidemiological Review (TMER), by the National CJD Surveillance Unit (NCJDSU) and the UK Blood Services (UKBS) to determine whether there is any evidence that Creutzfeldt–Jakob disease (CJD), including sporadic CJD (sCJD), familial CJD (fCJD), and variant CJD (vCJD) is transmissible via blood transfusion.

Materials and Methods Sporadic CJD and fCJD cases with a history of blood donation or transfusion are notified to UKBS. All vCJD cases aged > 17 years are notified to UKBS on diagnosis. A search for donation records is instigated and the fate of all donations is identified by lookback. For cases with a history of blood transfusion, hospital and UKBS records are searched to identify blood donors. Details of identified recipients and donors are checked against the NCJDSU register to establish if there are any matches.

Results CJD cases with donation history: 18/31 vCJD, 3/93 sCJD, and 3/5 fCJD cases reported as blood donors were confirmed to have donated labile components transfused to 66, 20, and 11 recipients respectively. Two vCJD recipients have appeared on the NCJDSU register as confirmed and probable vCJD cases. The latter developed symptoms of vCJD 6.5 years and 7.8 years respectively after receiving non-leucodepleted red blood cells (RBCs) from two different donors who developed clinical symptoms approximately 40 and 21 months after donating. A third recipient, given RBC donated by a further vCJD case approximately 18 months before onset of clinical symptoms, had abnormal prion protein in lymphoid tissue at post-mortem (5-years post-transfusion) but had no clinical symptoms of vCJD. CJD cases with history of transfusion: Hospital records for 7/11 vCJD and 7/52 sCJD cases included a history of transfusion of labile blood components donated by 125 and 24 donors respectively. Two recipients who developed vCJD were linked to donors who had already appeared on the NCJDSU register as vCJD cases (see above). No further links were established.

Conclusion This study has identified three instances of probable transfusion transmission of vCJD infection, including two confirmed clinical cases and one pre- or sub-clinical infection. This study has not provided evidence, to date, of transmission of sCJD or fCJD by blood transfusion, but data on these forms of diseases are limited.

Key words: blood, CJD, familial, sporadic, transfusion variant.

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Introduction

Until 2004, it was generally accepted that Creutzfeldt–Jakob disease (CJD) had not been transmitted by blood transfusion.

Preliminary findings from sheep studies indicate that bovine spongiform encephalopathy (BSE) and scrapie can be transmitted by blood transfusion [1,2]. It is vital to find out whether this also applies to human transmissible spongiform encephalopathies (TSEs) and, in particular, variant CJD (vCJD). The UK is the only country where a significant outbreak of vCJD has occurred and is in a unique position to study this question which has important implications for public health policy. The results reported in this paper are from a study which is being carried out, with ethical approval, to investigate whether or not there is any evidence for the transmission of any type of CJD (sporadic, familial and variant) by blood transfusion.

Materials and methods

CJD surveillance

A surveillance system for CJD, the National CJD Surveillance Unit (NCJDSU), was established in the UK in 1990 with the aim of identifying all cases of CJD in the UK. The methodology of this study has been described previously [3], but in brief involves referral of suspected cases to the Unit from targeted professional groups, including neurologists and neuropathologists, review of suspects by a neurologist from the Unit and review of investigation results and neuropathological material when available. Cases are classified according to standard diagnostic criteria [4,5]. Onset of clinical symptoms for vCJD cases are estimated to the nearest month by NCJDSU on the basis of available clinical information. Details of past medical history, including blood donation or transfusion, are obtained from the family of suspected cases. Following the identification of vCJD in 1996 a collaborative study, the Transfusion Medicine Epidemiological Review (TMER), was established between the NCJDSU and UK Blood Services (UKBS) to search for evidence of transfusion transmission of CJD. The study was granted ethical approval by the local Research Ethics Committee.

Notification of CJD cases with a history of donation

Sporadic CJD (sCJD) and familial CJD (fCJD) cases with a history of blood donation are notified to UKBS retrospectively. For vCJD, all patients who are old enough to have donated blood (> 17 years of age) are notified to UKBS at diagnosis, whether or not there is a known history of blood donation. Upon receipt of notification from the NCJDSU, a search is made for donor records. Current computer databases and archived records (computerized and paper-based records where appropriate) based at individual blood centres are searched using name, date of birth, and previous addresses as identifiers. For CJD cases reported as blood donors, information on dates and places of donation is also used to help locate past donor records. Where donor records are found, all components produced and issued to hospitals are identified and their fate determined, as recorded in hospital blood transfusion laboratory records. Recipient details are then checked against the NCJDSU register to establish if there is a match between these individuals and patients who have developed CJD. Recipients details are also flagged with the Office for National Statistics (ONS) to establish date and certified cause of death.

Plasma used for UK fractionation

Independent of this study, and for regulatory reasons, all plasma derived from donations made prior to a diagnosis of vCJD is notified to UK fractionators so that appropriate actions can be taken.

Notification of CJD cases with a history of transfusion

Information provided by relatives of CJD cases with a previous transfusion history is also passed to UKBS, who then liaise with appropriate hospital blood transfusion laboratories. The laboratories identify whether transfusions took place at the time and place indicated, and, if so, identify the components transfused to the case. Details of donation numbers, component type and date transfused are passed back to the local blood centre and this information is used to identify the donors. Donor details are checked against the NCJDSU register and with ONS. For both donors and recipients, searches before 1980 are now impractical as most hospital records are no longer extant.

Related public health measures

The Department of Health (England) set up a committee (the CJD Incidents Panel) in 2000 to advise health authorities on the management of incidents where patients may have been put at risk of CJD through medical procedures. Cases where a blood donor or blood recipient has later developed vCJD have been referred to the Incidents Panel for consideration and further actions have been recommended and implemented. These further actions are outside the scope of this study and are not reported in this paper.

Results

vCJD cases with history of blood donation

Identification of donors

A total of 150 vCJD cases (out of a total of 160 cases on the NCJDSU register) who were old enough to have been potential blood donors have been notified to UKBS as of 1 March

Table 1 Recipients of blood donated by variant Creutzfeldt–Jakob disease cases by year and blood component transfused ($n = 66$)

Year of transfusion	Blood component transfused	Number of recipients
1980–1984	Whole blood	1
	Red blood cells	1
1985–1989	Red blood cells	2
1990–1994	Red blood cells	9
1995–1999	Whole blood	1
	Red blood cells	15
	Red blood cells – buffy coat depleted[a]	2
	Red blood cells – leucodepleted[b]	2
	Fresh frozen plasma	3
	Cryo-depleted plasma	1
	Cryoprecipitate	1
	Platelets (pooled)	1
2000–2004	Red blood cells – leucodepleted	23
	Fresh frozen plasma – leucodepleted	2
	Platelets (pooled, leucodepleted)	2

[a]Red cells with buffy-coat (containing most of the platelets and white cells) removed by centrifugation and physical separation.
[b]Red cells leucocyte-depleted by pre-storage filtration to $< 5 \times 10^6$/unit according to UK guidelines [6].

2006. Of these, 31 of 150 (21%) were reported to have been blood donors at various times in the past, although there is variation in the details of available information and the confidence of families in donation history.

Donor records were found for 24 vCJD cases, comprising 20 reported by relatives as blood donors and four additional cases with no reported donation history. Of these, 18 vCJD cases (12% of the total eligible to donate blood) were confirmed to have donated labile blood components, with the number of components made and issued for use in UK hospitals ranging from 1 to 14 per donor. Six vCJD cases were registered as donors, but had not donated labile blood components. Two of these had never attended sessions, three were deferred (due to past medical history, low haemoglobin value and illness, respectively) and one case had donated plasma for fractionation only (made from a single donation from which the red cells were discarded).

The search for donor records was negative in 11 of 31 (35%) vCJD cases reported as putative donors (three of whom allegedly donated well before the onset of the BSE epidemic in the 1980s). The information provided in these negative cases was minimal, except in one case where relatives were confident that regular donations (up to 50) had been made in the years leading up to 1993. Despite extensive searches no records were found; moreover, blood collection sessions had never been made at the purported venue. No explanation has been found for the lack of records, although discrepancies in some of the details given suggest that the history was not as certain as initially thought.

Labile components issued to hospitals

Sixty-six labile components originating from 18 donors were issued to UK hospitals over the period 1981–2004 and transfused to patients according to blood transfusion laboratory records. A further nine components issued between 1982 and 1996 could not be traced by the relevant hospital. Table 1 gives the number of recipients transfused by year and the type of blood component transfused. Fifty-six recipients (85%) received red cells or whole blood, seven (11%) were transfused with labile plasma components or derivatives and three (4%) received pooled platelets made according to UK specifications in which the buffy-coat preparation containing platelets from the implicated vCJD donor was pooled with buffy coats from three other donors and resuspended in plasma from one of the four donations. Nearly half of the red cell recipients received red cells that had been leucocyte-depleted by pre-storage filtration to $< 5 \times 10^6$ leucocytes per unit (in 99% of units with 95% statistical confidence according to UK guidelines [6]) after the introduction of universal leucocyte depletion of the UK blood supply in 1999.

Recipients of blood components

Patient identifiers are available for 66 recipients who received blood from 18 different donors who went on to develop vCJD. None of the 66 recipients had themselves donated blood between receiving their transfusion and early 2004 when the UKBS implemented a policy of excluding all donors transfused in the UK since 1 January 1980. It is of note that 41 (62%) recipients were aged over 60 years at the time of transfusion and were not eligible to donate. All living recipients ($n = 26$) have been informed of their risk and advised not to donate blood, tissues or organs. Three instances of probable transfusion transmitted vCJD infection have occurred, including two confirmed clinical cases and one pre- or subclinical infection. Of these, two cases have died, and one is still alive (see succeeding discussion). Figures 1 and 2 show the survival period for dead (transfusion to death) and live recipients (transfusion to 1 March 2006) of vCJD components, respectively, according to the interval between transfusion and onset of clinical symptoms in the donor.

Dead recipients

Forty recipients (61%) are known to be dead, with mean age at death 66 ± 19 years. Table 2 gives the time and cause of death as stated on death certificates for the recipients known to have died. Around half ($n = 21$) of the dead recipients died within a year of receiving their transfusion, with only seven surviving for more than 5 years. Two recipients, who died 4 months and 14 months, respectively, after transfusion had

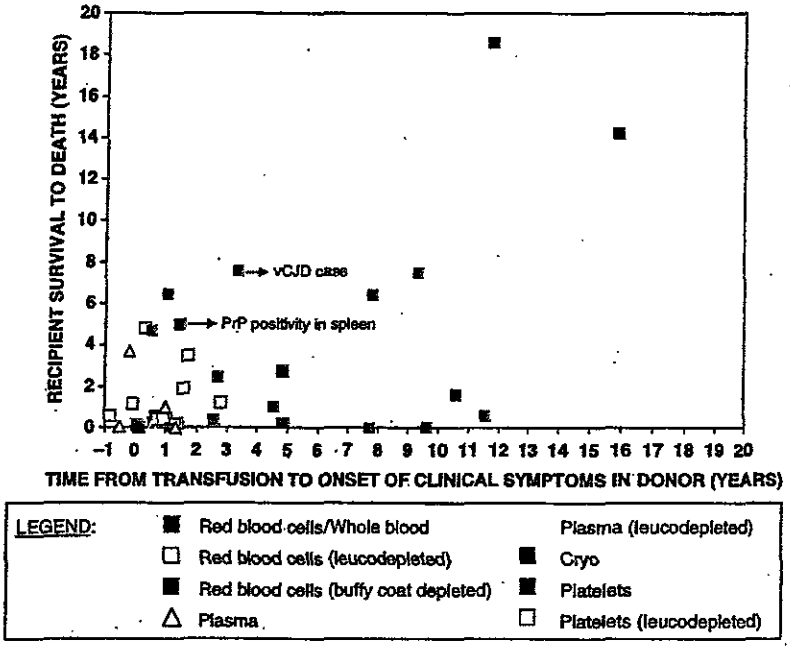

Fig. 1 Survival period (transfusion to death) for recipients of variant Creutzfeldt–Jakob disease components according to interval between transfusion and onset of clinical symptoms in the donor.

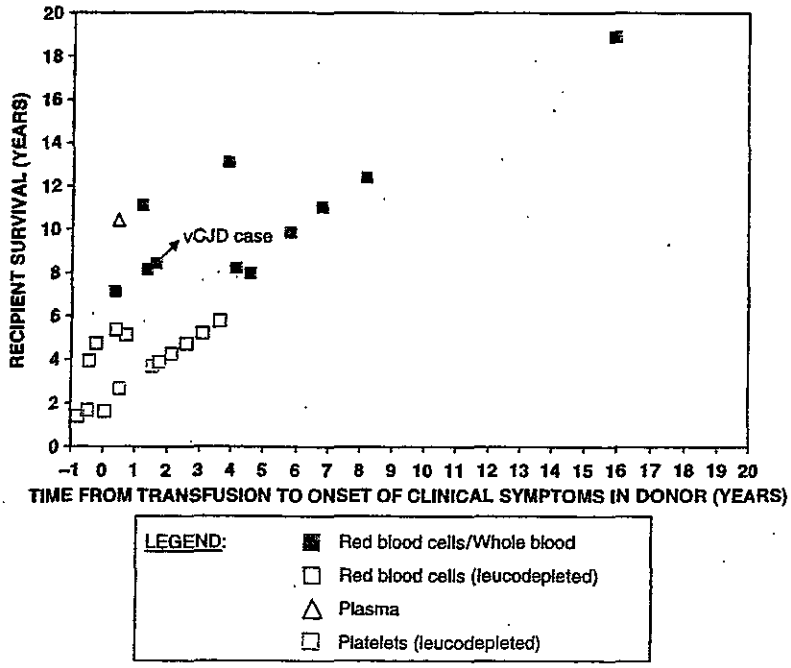

Fig. 2 Current survival period (since transfusion to 1 March 2006) for recipients of variant Creutzfeldt–Jakob disease components according to interval between transfusion and onset of clinical symptoms in the donor.

'dementia' recorded on the death certificate, but examination of case notes indicated that neither case had features to suggest vCJD. All the other recipients were certified as dying of causes unrelated to vCJD, except for a recipient whose cause of death on the death certificate was recorded as '1A dementia and II. prostate cancer' and was later confirmed neuropathologically as suffering from vCJD [7]. This patient, who had received a transfusion of red cells 6.5 years before onset of clinical symptoms, was a methionine homozygote at codon 129 of the human prion protein gene (*PRNP*). The case that donated to this individual also had a neuropathological diagnosis of vCJD, with clinical onset approximately 40 months after donating. In a second red cell recipient (of a different donor who developed clinical symptoms approximately

Table 2 Cause of death of variant Creutzfeldt–Jakob disease recipients known to have died ($n = 40$)

Interval from transfusion to death	Number of recipients	Cause of death
< 1 month	7	Acute renal cortical necrosis
		Cancer (2)
		Myocardial infarction
		Septicaemia (2)
		Sepsis (pancreatitis)
1– < 6 months	11	Aspiration pneumonia (sigmoid resection)
		Cancer (4)
		Myelodysplasia (2)
		Myelofibrosis
		Peritonitis (2)
		Stroke/diabetes mellitus/dementia
6– < 12 months	3	Cancer (3)
1– < 5 years	12	Acute myeloid leukaemia (2)
		Bronchopneumonia/senile dementia
		Cancer
		Ischaemic heart disease (3)
		Chronic obstructive airways disease (COAD)
		Hypertensive heart disease, chronic renal failure
		Myelodysplasia
		Disseminated sepsis
		Spinal haemangioblastoma
5– < 10 years	5	Cerebrovascular accident
		Ischaemic heart disease
		Acute lymphoblastic leukaemia
		Dementia[a], prostatic cancer
		Ruptured aortic abdominal aneurysm/severe atheroma/COAD[b]
≥ 10 years	2	Bronchopneumonia
		Ischaemic heart disease

[a]Confirmed variant Creutzfeldt–Jakob disease case [7].
[b]PrP positivity in lymphoid tissue, pre- or subclinical vCJD infection [8].

18 months after donating and was later diagnosed with neuropathologically confirmed vCJD), protease-resistant prion protein (PrP^{res}) was detected in the spleen and one lymph node (but not in the brain) at post-mortem [8]. This recipient, who died 5 years after transfusion without any clinical symptoms of vCJD, was a codon 129 *PRNP* heterozygote and is thought to represent pre- or subclinical infection.

Live recipients

Twenty-six recipients (39%) are alive as of 1 March 2006 with a mean age of 63 ± 19 years. Table 3 shows the number of live recipients according to the time elapsed since transfusion, along with their current age, component transfused and the interval between donation and onset of clinical symptoms of vCJD in the donor. Fifty per cent of live recipients were transfused with components from vCJD donors whose donations were made within 20 months of clinical onset, in seven cases around the time of development ($n = 3$) or shortly after ($n = 4$) the first signs of clinical illness. These cases would have appeared healthy when attending donor sessions and passed the normal medical checks as being fit to donate. Sixteen recipients have survived longer than 5 years, with six surviving > 10 years (one for over 18 years). These patients, mean age currently 61 ± 19 years, were given blood from donors who developed vCJD symptoms at intervals ranging from around 5 months to 191 months after making the donation (see Table 3). Recently, a diagnosis of probable vCJD has been made in one of these surviving recipients who had received a transfusion of red cells 7 years and 10 months before onset of clinical symptoms [9]. The donor of this third probable transfusion-transmitted vCJD infection developed vCJD approximately 21 months after the donation, and the recipient is a codon 129 *PRNP* methionine homozygote.

Plasma for UK fractionation

Twenty-five units of plasma originating from 11 different donors, bled between 6 months and 17 years, 11 months before onset of clinical vCJD symptoms, were supplied for UK fractionation during the period 1986–1998. Product batches manufactured from 23 plasma units derived from nine donors have been traced. The fate of batches of product derived from the two remaining plasma donations, from two different donors, has not yet been traced, and this search is still ongoing. Table 4 lists the plasma products derived from the 23 traced donations and the number of batches implicated, divided into risk categories as used in the plasma product notification exercise (www.hpa.org.uk/infections/topics_az/cjd/Recommendations.pdf). The fate of batches of products has not been traced to individual recipients as part of this study. It is known, however, that haemophilia centres have traced the ultimate fate of the batches of factor VIII. It is also known that no case of vCJD has been identified in a patient with haemophilia in the UK.

sCJD cases with history of blood donation

Ninety-three cases of sCJD identified between 1980 and 2000 were reported to have been blood donors, with only 38 reported to have donated from 1980 onwards. Donation records for most sCJD cases were untraceable since most dated back many years before 1980, in some cases to the 1940s. Donation records were found for eight sCJD cases, but only three had actually donated labile blood components for hospital use (one with 18 recipients, and one each with one recipient) which could be traced to recipients. A total of 20 recipients were transfused between 1995 and 1999 with components from these three donors who went on to develop

Table 3 Live recipients of labile blood components donated by variant Creutzfeldt–Jakob disease cases ($n = 26$)

Time elapsed since transfusion[a]	Current age of recipient (years)[a]	Blood component transfused	Interval between blood donation and onset of clinical symptoms in donor (months)[b]
1 – < 2 years	48	Platelets (leucodepleted)	–9 months
	49	Red cells (leucodepleted)	–5 months
	83	Red cells (leucodepleted)	2 months
2 – < 3 years	38	Red cells (leucodepleted)	7 months
3 – < 4 years	58	Red cells (leucodepleted)	19 months
	83	Red cells (leucodepleted)	22 months
	90	Red cells (leucodepleted)	–5 months
4 – < 5 years	59	Red cells (leucodepleted)	26 months
	67	Red cells (leucodepleted)	–2 months
	89	Red cells (leucodepleted)	32 months
5 – < 6 years	30	Red cells (leucodepleted)	37 months
	52	Red cells (leucodepleted)	9 months
	64	Red cells (leucodepleted)	44 months
	71	Red cells (leucodepleted)	5 months
6 – < 7 years	–	–	–
7 – < 8 years	42	Red cells	5 months
8 – < 9 years	31[c]	Red cells	21 months
	74	Red cells	17 months
	76	Red cells	49 months
	87	Red cells	55 months
9 – < 10 years	75	Red cells	70 months
> 10 years	33	Cryo-depleted plasma	7 months
	49	Red cells	15 months
	67	Red cells	46 months
	70	Red cells	191 months
	75	Red cells	98 months
	87	Red cells	82 months

[a]As at 1 March 2006.

[b]A negative interval denotes that donation was made by individual while (retrospectively recognized) clinical symptoms were present.

[c]Probable variant Creutzfeldt–Jakob disease case [9].

sCJD between 1 and 5 years after donation. Of these, 11 (55%) received red cell components, eight recipients (40%) received platelets and one (5%) received fresh frozen plasma.

As of 1 March 2006, 12 recipients are confirmed dead with a mean age at death of 74 ± 15 years. Of these, five died soon after transfusion (four within a week, and one 2 months later) and seven survived for between 1 and 8 years after receiving their transfusion before dying of a variety of non-CJD-related causes (cerebrovascular accident/stroke, $n = 3$; acute myeloid leukaemia, $n = 3$, general debility/old age, $n = 1$). Seven recipients are not known to be dead from ONS flagging to date, and are therefore presumed to be alive. The mean age of these seven recipients is 58 ± 19 years. The time elapsed since their transfusion ranges from 7 to 9 years. The fate of a further recipient is unknown. None of the sCJD recipients identified as having received blood from donors who went on to develop sCJD have appeared on the NCJDSU register to date.

fCJD cases with history of blood donation

Donation records were found for three out of five cases of fCJD identified between 1992 and 2000, all reported to have donated blood after 1980. These three cases had all donated labile blood components (one with five recipients, one with four recipients and one with two recipients) for hospital use which could be traced to individual recipients. A total of 11 recipients were transfused between 1977 and 1992 with labile components from these three donors who went on to develop fCJD between 1 and 15 years later. Nine of the 11 (82%) recipients received red cell components (whole blood $n = 6$, red cells $n = 3$) while two received platelets.

Five of 11 recipients identified have since died with a mean age at death of 75 ± 6 years. Three of these survived for 3, 10 and 17 years after transfusion before dying of non-CJD-related causes (cancer, $n = 2$; bronchopneumonia, $n = 1$); and two died of cancer shortly after receiving their transfusion.

