Table. Estimated range of incubation periods for variant Creutzfeldt-Jakob disease cases with presumed route and year of exposure*

<table>
<thead>
<tr>
<th>Presumed route of exposure and country of residence</th>
<th>Period of potential BSE/vCJD exposure</th>
<th>Estimated range of incubation period (y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foodborne</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canada</td>
<td>1987–1990</td>
<td>11–14</td>
</tr>
<tr>
<td>Ireland</td>
<td>1980–1995</td>
<td>5–10</td>
</tr>
<tr>
<td>Japan</td>
<td>1980</td>
<td>12</td>
</tr>
<tr>
<td>United Kingdom (Leicestershire, England)</td>
<td>1980–1985</td>
<td>10–16</td>
</tr>
<tr>
<td>United States</td>
<td>1980–1992</td>
<td>9–21</td>
</tr>
<tr>
<td>Bloodborne</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Kingdom</td>
<td>1996</td>
<td>6.5</td>
</tr>
<tr>
<td>United Kingdom§</td>
<td>1999</td>
<td>&gt;5</td>
</tr>
</tbody>
</table>

*BSE/vCJD, bovine spongiform encephalopathy/variant Creutzfeldt-Jakob disease.
†Estimated range of incubation periods are based on a single vCJD case except for Leicestershire, England, where the Leicestershire Health Authority reported the estimated incubation period for a cluster of 5 vCJD cases.
§Patient was reported to have stayed in the United Kingdom ≤24 days.
¶Patient with presumed bloodborne transmission died of a nonneurologic disease. The presence of the vCJD agent was detected in the spleen and cervical lymph node; the patient was heterozygous for methionine and valine at the polymorphic codon 129 of the prion protein gene.

The second patient potentially linked with bloodborne transmission of vCJD was an elderly person who received a unit of erythrocytes in 1999. vCJD developed in the donor of the unit 18 months after blood was donated (6). The recipient died of a ruptured aortic aneurysm 5 years after the transfusion. Tests of the patient’s spleen and cervical lymph node detected protease-resistant prion protein with a Western blot mobility pattern and glycoform ratio similar to those seen in other vCJD patients. These results and the absence of neurologic symptoms and brain pathologic findings indicated that this patient had a subclinical vCJD infection. Prion protein gene sequencing showed heterozygosity for methionine and valine at codon 129, which indicated that persons not homozygous for methionine (>50% of the population) can be infected by the vCJD agent.

In the United States, the risk of bloodborne transmission of vCJD is low because of the absence of indigenous vCJD and the geographic-based donor deferral policy instituted by the Food and Drug Administration in 1999. This policy excludes from donating blood in the United States persons who resided in or had extended visits to the United Kingdom or other European countries during periods of greatest concern for BSE exposure (7).

The exact incubation period for foodborne vCJD is unknown. However, a range of possible incubation periods was estimated for 4 vCJD patients who likely acquired the disease during their residence in the United Kingdom and for 5 vCJD patients reported as part of a cluster in Leicestershire, England (Table). The median of the estimated range of incubation periods for these 9 vCJD patients was 13 years. The incubation period for the vCJD patient linked to bloodborne transmission was shorter (6.5 years). This finding could be the result of direct transmission of the agent into the bloodstream and adaptation of the agent to the human population, thus reducing or eliminating the species barrier (Table).

Conclusions

Patients with vCJD can be distinguished from patients with the more common sporadic CJD by their younger median age at death (28 years and 68 years, respectively), predominantly psychiatric manifestations at illness onset, delayed appearance of frank neurologic signs, absence of a diagnostic electroencephalographic pattern, presence of the pulvinar sign on MRI, and a longer median illness duration (<6 and 14 months, respectively) (3,8). Almost all vCJD patients have died before 55 years of age, compared with only ~10% of sporadic CJD patients. The most striking early neurologic manifestation in some vCJD patients was painful sensory symptoms (dysesthesia or paresthesia). Other neurologic signs, such as chorea, dystonia, and myoclonus, commonly develop late in the course of vCJD. An MRI result with symmetrically increased signal intensity in the pulvinar region relative to the signal intensity in other deep and cortical gray matter areas has been reported in >75% of vCJD patients. The presence of this MRI feature, known as pulvinar sign, may suggest a vCJD diagnosis in the appropriate clinical context. A prominent, early involvement of lymphoid tissues has enabled a reasonably accurate premortem diagnosis of vCJD, using tonsillar biopsy. However, a more definitive

![Figure 3. Number of deceased variant Creutzfeldt-Jakob disease patients worldwide (150 from the United Kingdom and 15 outside the United Kingdom) by year of death, June 2005.](image_url)
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diagnosis of vCJD may require testing autopsy brain tissues.

In June 2005, the US Department of Agriculture confirmed BSE in an 112-year-old cow born and raised in Texas. This is the first time an indigenous BSE case was detected in the United States. A previous BSE-positive cow identified in Washington State was imported from Canada (3) where, to date, 4 additional BSE cases have been identified. The identification of BSE in North America and the likelihood of bloodborne transmission of vCJD underscore the need to continue surveillance to monitor the occurrence of vCJD in the United States (3). The case-patient described in this report illustrates the need for physicians to remain vigilant for the possibility of vCJD in patients with the signs and symptoms described. Physicians should report suspected vCJD cases to local and state health departments. Because the clinical manifestation of vCJD can overlap that of sporadic CJD, brain autopsies should be sought in all suspected cases to establish the diagnosis and to help monitor the occurrence of vCJD and other potentially emerging forms of CJD. Free state-of-the-art prion disease diagnostic testing is available from the National Prion Disease Pathology Surveillance Center (http://www.cjdsurveillance.com), which was established to facilitate autopsy performance and testing (8). Physicians are encouraged to use the services of the surveillance center to evaluate neuropathologic changes in their patients with suspected or clinically diagnosed prion disease.

Acknowledgments

We thank the patient’s family and the Broward County Health Department for facilitating the case investigation, and Jeltley Montague, Jeanine Bartlett, and Tara Jones for assisting with tissue processing and immunohistochemical staining.

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References


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医薬品 研究報告 調査報告書

<table>
<thead>
<tr>
<th>識別番号・報告回数</th>
<th>報告日</th>
<th>第一報入手日</th>
<th>新規薬品等の区分</th>
<th>総合機構処理欄</th>
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<tr>
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<td>公表国</td>
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<td>販売名（企業名）</td>
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<table>
<thead>
<tr>
<th>研究報告書の概要</th>
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| 輸血および外科手術による変異型クローンツフェルト・ヤコブ病（vCJD）伝播のリスクを減少させるための予防措置が拡大された。vCJDを発症した3名の受血者に供血した約100名の供血者は、他の人々と比べvCJD因子を保有している可能性が高い。
これらの供血者は、血液、組織、および器官を供与しないよう求められ、また、万一外科手術等をする場合には、特別な予防措置が講じられるよう、医師等に通知するよう要請された。
3名の患者におけるvCJDの発生源が、これらの供血された血液と関係があるかどうかははっきりしないが、公衆衛生を守るだけでなく、個人に通知してサポートするためにもこの予防措置は講じられた。
vCJD伝播の可能性を除外するための信頼できる血液スクリーニングテストが利用できるようになるまで、このような予防措置を続行する。|

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<tr>
<th>報告企業の意見</th>
<th>今後の対応</th>
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<tbody>
<tr>
<td>受血後にvCJDを発症した3名に対し、血液を提供していた供血者は、他の人々と比べvCJD因子を保有している可能性が高いので、今後の供血、組織提供等を行わないよう通知したとの情報である。</td>
<td>今後ともvCJDに関する安全性情報、規制情報等に留意していく。</td>
</tr>
</tbody>
</table>
Notification exercise begins to reduce risk of vCJD transmission

Published:  
Wednesday 20 July 2005  
Reference number:  
2005/0256

An extension to the precautionary measures to reduce the risk of transmitting vCJD through blood transfusion and surgical procedures, began today. Around 100 people who donated blood to three people who later developed vCJD, are being told that they may have a greater chance of carrying the vCJD agent, compared with the general population.

They will be asked not to donate blood, tissue or organs and to inform health professionals so extra precautions can be taken should they have surgery or other invasive procedures.

Although it is not known whether the source of vCJD in these patients is related to the blood that they received, precautionary steps are being taken to inform and provide support to the individuals as well as safeguard public health. This is being done on the advice of two expert committees and a detailed risk assessment exercise.

Notification of donors is taking place via letters from the National Blood Service who are working closely with the Health Protection Agency to identify the people involved. The letters that people receive will provide the telephone number for a dedicated helpline staffed by senior transfusion experts from the National Blood Service, and will also advise them to contact their GP for more information, advice and support.

The likelihood of a person who may be infected with vCJD going on to develop symptoms of the disease is uncertain. It is possible that an infected person may never develop symptoms.

The Chief Medical Officer, Sir Liam Donaldson said:

""We need to ensure that appropriate action is taken on any new information that becomes available on the risk of transmission of vCJD, to protect the public as much as possible. When a recipient of a blood transfusion goes on to develop vCJD, we have to consider the possibility that the infection could have been passed on through the transfusion."

""Until a reliable blood screening test becomes available, it is sensible to proceed with highly precautionary measures such as this to rule out any possibility of onward transmission of the disease. We are committed to further research to help us understand this disease and diagnose infection at an early stage."

""Following the identification of vCJD, we introduced a number of measure to reduce the possible risk that infection could be transmitted through the blood supply. Since the announcement in December 2003 of the first case of possible transfusion-associated transmission of vCJD, we have further strengthened these preventative measures. The decisions taken so far have been based on the principles of caution and openness. This announcement today is a continuation of the process."

Dr Angela Robinson from the National Blood Service said:

""Blood donors are highly committed to helping other people and we greatly value their contribution. The NHS depends upon their continued commitment in order to be able to save lives."

""This notification exercise will affect the in the order of 100 donors. If you have donated blood in the last five years and are not contacted shortly, you can be assured that you are not involved in this new safety measure and need to take no further action."

1/2
lotification exercise begins to reduce risk of vCJD to...

"For those people who are involved, this information may be difficult to absorb. That is why we have set up the National Blood Service helpline and are working with their doctors and other clinicians, to ensure that they have the information and support they need."

Related links

CJD

Notes to editor

1. This notification exercise has been done after a detailed risk assessment by the Department of Health and reviewed by its relevant expert committees. The risk assessment can be found on the DH website.

2. The degree of increased risk for any individual donor depends on many factors, including how many other donors' blood went to the infected recipient. This varies very widely between these three recipients. Individual donors will be able to find out more if they wish.

3. Of the 156 cases of vCJD to date, 4 have been confirmed as having had blood transfusions that experts believe could be linked with their vCJD. For one of these cases, the probable source of infection has already been identified, as one of the donors went on to develop vCJD. For three cases, transfusion remains a possible source of the recipient's infection.


5. The two expert committees advising this course of action were the CJD Incidents Panel and the Committee on the Microbiological Safety of Blood Tissues and Organs.

6. Previous measures taken to improve the safety of blood in relation to vCJD include the following:

   - From December 1997, blood components, plasma products or tissues obtained from any individual who later develops vCJD, have been withdrawn/recalled.
   - In July 1998, we announced that plasma for the manufacture of blood products, such as clotting factors, would be obtained from non-UK sources.
   - From November 1999, white blood cells (which may carry a significant risk of transmitting vCJD) have been removed from all blood used for transfusion.
   - In August 2002 we announced that fresh frozen plasma for treating babies born on or after 1 January 1996 would be obtained from the USA.
   - The report of the first possible case of transmission of vCJD by blood transfusion was in December 2003. Following this, we announced in April 2004 that individuals in themselves received a transfusion of whole blood components since January 1980, would be excluded from donating blood. (In July 2004, the second possible case of transmission of vCJD by blood transfusion was reported.)
   - In July 2004, the exclusion criteria for blood donation were extended to include two new groups, who had received transfusions of whole blood components since 1980:
     - Previously transfused platelet donors
     - Donors who were unsure if they had previously had a blood transfusion.

This means that for blood donation the full exclusion criteria are:

- Recipients of dura mater grafts.
- Recipients of corneal or scleral grafts.
- Recipients of human pituitary derived extracts such as growth hormone or gonadotrophins.
- Individuals at familial risk of prion-associated diseases. This includes individuals who have had two or more blood relatives develop a prion-associated disease and individuals who have been informed they are at risk following genetic counselling.
- Individuals who had themselves received a transfusion of whole blood components since January 1980 are excluded from donating blood.
- Individuals identified as 'at risk' by CJD Incidents Panel.
- Previously transfused platelet donors.
- Donors who were unsure if they had previously had a blood transfusion.

In September 2004, the Department of Health announced further precautionary measures for patients who have received certain batches of plasma products.

In July 2005 the use of USA sourced fresh frozen plasma (FFP) was extended to all children up to the age of 16.

7. There is currently no validated diagnostic test that can be used before the onset of clinical symptoms to diagnose whether someone has contracted vCJD. Since 1995, the Department has contributed over £30 million into CJD research, including research for the development of an effective test.

8. For media enquiries only contact Sophie Coppel in the Department of Health Media Centre on 020 7210 5707.