

Minutes of the 16th meeting of the CJD Incidents Panel

Wednesday 7th September 2005, BMA House, London

Chairman	Expertise
Mr David Pryer	Lay member
Deputy Chairman	
Professor Don Jeffries	Virology
Members	
Mr John Barker	Sterile Service Management
Professor Mike Bramble	Gastroenterology
Dr Gerry Bryant	Public Health Medicine
Ms Patricia Cattini	Infection Control Nursing
Dr Geoff Craig	Dental Surgery
Dr Bobbie Farsides	Ethics
Mrs Jean Gaffin	Lay Member
Dr Pat Hewitt	Blood Safety
Professor James Ironside	TSE Infectivity, Neuropathology
Ms Diana Kloss	Law
Professor John Lumley	General Surgery
Dr Bernadette Nazareth	Communicable Disease Control
Dr Mike Painter	Public Health Medicine
Mr Ian Pearce	Ophthalmology
Dr Geoff Ridgway	Microbiology
Dr Roland Salmon	Epidemiology
Dr John Saunders	Medical Ethics
Ms Gillian Turner	Lay Member
Dr Hester Ward	Epidemiology
Dr Tim Wyatt	Microbiology

Observers	
Dr Peter Bennett	ESOR, Department of Health
Dr Stephen Dobra (for items 9 and 10)	ESOR, Department of Health
Ms Carole Fry	Nursing Officer, Department of Health
Dr Rowena Jecock	Health Protection, Department of Health
Secretariat	
Professor Noel Gill	Health Protection Agency Centre for Infections
Ms Helen Janecek	Health Protection Agency Centre for Infections
Ms Katie Oakley	Health Protection Agency Centre for Infections
Dr Kate Soldan	Health Protection Agency Centre for Infections
Apologies	
Professor Adam Balen	Obstetrics and Gynaecology
Dr Peter Christie	Scottish Executive Health Department
Professor Lesley Fallowfield	Communication with Patients
Mr Henry Marsh	Neurosurgery
Dr Elizabeth Mitchell	DHSSP, Northern Ireland
Dr Douglas Russell	General Practice
Dr Mike Simmons	National Assembly of Wales
Dr Peter Simpson	Anaesthesia
Professor Bob Will	Neurology
Ms Kate Woodhead	Theatre Nursing

1. Welcome and apologies (CJDIP 16/01)

The Chairman welcomed participants to the meeting and announced apologies from the members listed above.

2. Minutes of the 15th meeting on 11th May 2005 (CJDIP 16/02)

The minutes of the previous meeting were agreed, subject to changing the title of item 5.i to “TSE exposures in occupational health settings”.

3. Public summary of 15th meeting on 11th May 2005 (CJDIP 16/03)

The Panel approved the draft public summary of the previous meeting, subject to changing the title of item 3.i to “TSE exposures in occupational health settings”.

4. Panel appointments

The Chairman welcomed Dr Bernadette Nazareth as the new consultant in communicable disease control (CCDC) member to her first meeting. She had been selected with the assistance of the Public Health Medicine Environmental Group.

5. Matters arising

5.i TSE exposures in occupational settings

It was reported that the Health Protection Agency (HPA) had been asked by the Department of Health (DH) to submit an outline proposal for surveillance of TSE exposures in occupational settings to be discussed further by the DH and the Health and Safety Executive.

5.ii Dentistry (CJDIP 16/04a,b)

The Panel noted the letter dated 20th June to the Scottish Executive in response to their enquiry concerning the reprocessing of surgical instruments used on ‘at risk’ patients in the light of the report on decontamination in dentistry in Scotland. This stated that the Panel’s advice remains unchanged as ‘high street’ dental procedures are considered to be low risk.

Dr Craig was thanked for drafting an advice note concerning problems with accessing dental care for individuals ‘at risk’ of CJD. The statement had been developed with assistance from the UK Haemophilia Centre Directors’ Association and was intended to be used reactively by the HPA. Including it in information materials to all ‘at risk’ individuals was felt to be unnecessary and might cause avoidable anxiety about accessing routine dental care. The wording of the statement needed to reflect the arrangements in the four UK countries and might need updating when the contractual

arrangements for primary care dentistry change with effect from 1st April 2006. This note will be provided to the CJD Support Network (and others) who deal with queries from patients. It was suggested that local Patient Advice and Liaison Services could be made aware of the advice note for 'at-risk' patients having problems accessing dental services.

ACTION: Secretariat, HPA

5.iii Letter to UK Xenotransplantation Interim Regulatory Authority (CJDIP 16/04c)

The Panel noted the letter dated 17th August to the UKXIRA Secretariat informing them of the forthcoming publication of a paper which includes a report of the first known case of CJD in a recipient of porcine dura mater graft applied during a neurological procedure. (As reported at the previous meeting, the case is thought to most probably be coincidental with graft receipt.)

5.iv Revised TSE Working Group guidance on endoscopes

It was reported that the third revision since 2003 of Annex F to the guidance would be published following approval by the British Society of Gastroenterology Decontamination Subgroup and the Advisory Committee on Dangerous Pathogens (ACDP). The Annex now contains an extensive table categorising endoscopic procedures according to the risk of contamination of the endoscope. Dr Bramble, Dr Painter and Dr Hewitt were thanked for their contributions to the revised guidance and to a consensus statement that has been prepared to describe and publicise it.

6. Quarterly summary of reported incidents (CJDIP 16/05)

It was noted that 53 incidents had been reported to the Panel from January to July 2005, compared with 17 for January to June 2004. A larger proportion of incidents now related to 'at-risk' patients as a result of patient notification exercises recommended by the Panel. Cataract operations on patients with sporadic CJD form another consistently large proportion of incidents.

7. Discussion and endorsement of advice provided since 11th May 2005

7.i Incidents involving contactable patients (CJDIP 16/06a)

The Panel endorsed the advice given in relation to the following incidents:

Panel advice that patients should be contacted

**PI 339 Probable sporadic CJD – Procedure: cataract removal
Letters reviewed: PI 339-2 draft, PI 339-1 final**

The Panel would advise that the first two patients on whom the instrument set had been used should be informed of their exposure and asked to take special public health precautions.

Incidents where patients may be contactable

It was reported that further information was awaited to enable the Panel to advise on whether patients in the following incidents needed to be contacted:

PI 271 Probable sporadic CJD – Procedure: right cataract extraction 2003
Letter reviewed: PI 271-3 final

Previous Panel advice that the first two subsequent patients on whom instruments had been used for a left cataract extraction should be contacted has been implemented. Further advice had been sought concerning a right cataract extraction. To date insufficient information had been provided to justify notifying patients in relation to the right cataract extraction.

PI 340 ‘At-risk’ vCJD due to receipt of implicated blood components – Procedures: 11 laparotomies and 30 oesophageal dilatations
Letter reviewed: PI 340-1final

PI 341 ‘At-risk’ vCJD due to receipt of implicated blood components – Procedure: colonoscopy with 5 biopsies
Letter reviewed: PI 341-1 final

With reference to PI 340 and PI 341, the Panel agreed with the proposal of the subgroup that subsequent patients on whom potentially contaminated instruments had been used for non-invasive endoscopic procedures should not be notified, and that this could be used as a precedent for future similar incidents. The Secretariat had reviewed past incidents: for one incident (PI267) this new precedent may result in revision of Panel advice issued. The local team will be asked for further information.

It was noted that it is important to distinguish between incidents involving instruments which have undergone more than 10 complete cycles of use and satisfactory washing and decontamination where it has become practice to advise retrospectively, on the basis of pragmatism, that the instruments need not be removed from use, and incidents where decontamination was sub-standard and instruments may need to be considered on a case by case basis, even after more than 10 cycles of use and decontamination.

PI 349 Definite sporadic CJD – Procedure: argon laser therapy for diabetic retinopathy
Letter reviewed: PI 349-1 final

PI 329 Unclear, but to be considered as sporadic CJD – Procedures: Cataract surgery, left carpal tunnel decompression
Letters reviewed: PI 329-2 final, PI 329-1 final

7.ii Endorsement of advice provided (based on precedent) (CJDIP 16/06b)

Letters reviewed: PI 236-2 final; PI 273-2 final; PI 277-1 final; PI 278-3 final; PI 306-1 final; PI 316-1 final; PI 317-1 final; PI 318-1 final; PI 319-1 final; PI 320-1 final; PI 321-1 final; PI 322-1 final; PI 323-1 final; PI 327-2 final; PI 331-1 final; PI 333-1 final; PI 335-1 final; PI 336-1 final; PI 337-1 final; PI 338-1 final; PI 344-1 final; PI 346-1 final

The Panel endorsed the advice based on precedent in relation to incidents issued since the previous meeting and advice letters in relation to nine incidents which had been omitted from the papers for the previous meeting.

In view of the relatively large number of incidents involving cataract surgery and endoscopy, the question was raised whether the risk of vCJD transmission should be included in the patient consent process for these procedures. It was noted that these procedures are very common and the number of incidents was therefore an extremely small percentage of all procedures. The specifications for a complication deserving of inclusion in information discussed prior to consent were discussed. The Panel concluded that the risk of exposure to CJD (or involvement in an incident) should not necessarily be included in the consent process.* It was agreed that the emphasis should be on identifying patients at increased risk of CJD, or in the early stages of CJD, through pre-surgical assessment. It was reported to the Panel that an informal, limited survey of infection control nurses in SE England indicated that questions to identify 'at-risk' patients were not being included in pre-assessment for either elective or emergency surgical procedures. This issue of pre-assessment falls into the remit of the ACDP TSE Working Group and would be included in the agenda for the next meeting in November.

ACTION: Chairman of ACDP TSE Working Group

8. Notification of individuals 'at risk' of vCJD due to blood transfusion and donation

The Panel received a report from the HPA and NBS on progress with the implementation of Panel advice, approved by the UK Chief Medical Officers, to notify 'at-risk' individuals.

8.i Recipients of implicated blood components (April and July 2005)

Seventeen living recipients of blood components from 16 donors who had subsequently developed vCJD had been notified in winter 2003/2004. During 2005, following the diagnosis of vCJD in two more former donors, a further 10 living recipients of implicated blood components had been traced,

* The Royal College of Ophthalmologists' Cataract Surgery Guidelines 2004 state: "It is rarely a legal requirement to seek written consent but it is good practice to do so, especially if the cataract operation is complex or involves significant risks; the term 'risk' properly refers to any adverse outcome, including those which some health professionals would describe as 'side-effects' or 'complications'. There is no statistical 'threshold' for complications, below which it is not necessary to discuss the possibility of their occurrence with the patient; case law determines whether consent was truly informed."

notified and asked to take special public health precautions. This gives a total of 27 living blood transfusion recipients who have been notified, although one of these has since died. These notifications have resulted in a number of incidents being reported to the Panel, many involving gastro-intestinal procedures.

8.ii Donors to vCJD cases (notification status September 2005) (CJDIP 16/07)

Following on from the Panel recommendation made at the May meeting, the notification of donors to vCJD cases had been announced in the House of Commons on 20th July, the date on which 43 'active' donors (37 in England and Wales; 6 in Scotland) received letters from the UK Blood Services notifying them of their 'at-risk' status and of the public health precautions required. Notification of 12 more individuals subsequently identified as 'active' donors followed shortly. Notification of the remaining 'lapsed' donors (who had last donated blood over five years previously) was continuing as their current address and health status were checked, with fewer than 20 notifications outstanding by 9th September. For the first time in a patient notification exercise recommended by the Panel, 'at-risk' individuals were being informed by a letter (from the NBS/SNBTS) accompanied by a comprehensive information leaflet. It was reported that, on the whole, donors seemed to have received the news with equanimity. GPs had been very receptive to the process, and were supporting their patients proactively with the assistance of an information pack and their local Health Protection Unit (CCDC).

9. Recipients of blood components from donors to vCJD cases (CJDIP 16/08a,b)

The UK CMOs had accepted the recommendation from the May Panel meeting that donors to vCJD cases should be considered as 'potentially at-risk of vCJD for public health purposes' unless the estimated probability of being infected with vCJD (implied by donation to a vCJD case) was clearly below 1%. The CMOs now required further advice concerning the recipients of other donations from these donors. These recipients were already excluded from donating blood by the existing donor selection guidelines. Both donation and transfusion history would be reviewed should they develop vCJD (under the TMER protocol). However, the Panel needed to consider the risk-classification of these recipients; whether public health precautions relating to surgical instruments should be taken; and the potential value of monitoring these recipients to enhance the ascertainment of vCJD-related disease. For the three cases (nos. 1, 2 and 3) involving 'at-risk' donors (103, 3 and

4 respectively) before the Panel for consideration, there were an estimated 2830, 20 and 114 other blood donations respectively to consider.

The DH ESOR team had undertaken some additional analysis of the further implications of the 'reverse' blood risk assessment, to estimate the risks to the other recipients of donors to vCJD cases with different assumptions about the probability of transmissions of vCJD by transfusion. This showed that where the probability of transmission from a (potentially) infected donor is less than 1, the risk to the other recipients of their blood is reduced in two ways: the donor is less likely to have been the source of the infected recipient's disease (reverse risk assessment) and, even if the donor was the source, the chance of infection being passed on to another recipient is diminished (forward risk assessment). The calculation of risk, in scenarios involving both few and many other recipients depends on the value chosen for the probability of transmission (t). For the donors to vCJD cases, the risk of their being infected falls only slowly as t decreases and, in all cases to date, remains in the region of 1% (the usual threshold used by the Panel for patient notification in incidents) or higher. However, for the other recipients, the risk of their being infected falls more rapidly as t decreases, particularly where many donors are linked to an infected recipient. In the case of 3 donors linked to the infected recipient, the implied risk of transmission to the other recipients remains above 1% unless t is less than 0.1 (ie. blood from an infected donor assumed to have less than a 1 in 10 chance of infecting the recipient). Transfusion transmission studies on animals have shown a transmission rate (t) of approximately 0.25 – 0.35 (rising as experiments continue). In humans, there had been only two recipients investigated by post mortem: both had had vCJD infection. The transmission rate in humans might therefore be reasonably assumed to be anywhere between 0.35 and 1. This suggests a rationale for taking the precautionary approach of notifying the 'contacts of contacts' in this situation. Whereas the Panel does not advise notification of contacts of contacts in surgical incidents, there has been no known transmission of vCJD via surgical procedures and the probability of onward transmission via surgery may be lower.

Exploratory work by the NBS and their past experience of hepatitis C lookbacks, indicated that approximately two-thirds of the blood components from donors to vCJD cases are likely to be traced to transfused recipients: the records for the 1980s and early 1990s were not in current computer systems, but in either heritage or manual systems. Of those traced, 55% to 84% of

assumed recipients are likely to have documented confirmation in their medical records of having been transfused with the traced unit. Of the estimated 3,700 blood components issued for transfusion linked with the three index cases, it was further estimated that approximately 1,000 might be found to have been transfused into identifiable living recipients. This tracing exercise would be a large amount of additional work for NHS trusts, and might be perceived as having no tangible outcome. However, practical difficulties were regarded by the Panel as a consideration secondary to the primary aim of protecting the public health from further transmission of vCJD. There was extensive discussion concerning the further implications of the reverse risk assessment and the options concerning both the three cases before the Panel and potential future cases. Case no. 1 presented the most difficulty because it was estimated that approximately 3,500 blood components had been issued for transfusion and might lead to the notification of approximately 900 living recipients. It was thought that case nos. 2 and 3 would result in the notification of about 40 to 50 living recipients. The precedent set by case no. 1 was particularly important since it was understood that it was not unlikely that further cases of similarly large numbers would present to the Panel in future. A recommendation not to notify some or all of the other recipients but to include them in enhanced monitoring was dependent on approval by both the UK CMOs and a multi-centre research ethics committee (MREC) of the Panel's proposal for the establishment of monitoring of individuals with an identified low/uncertain risk. Comparison of the costs and benefits of notifying all the other recipients, including the anxiety caused to individuals, might indicate that the recipients linked to an index case with many donors should be subject only to enhanced monitoring. However, the Panel wished to see further work on this issue, including further consideration of the use of the 1% threshold in different cost:benefit situations.

It was agreed that the following should be recommended to the CMOs:

- i. For cases where the number of donors is low, and the implied risk for each other recipient is well **above** 1%, the Panel in general would advise that other recipients should be traced, informed of their potential exposure to vCJD and considered as 'potentially at-risk of vCJD for public health purposes'.

- ii. For cases where the number of donors is high (say, more than ~90), and the implied risk for each other recipient falls close to or **below** 1%, the Panel requests further risk assessment and discussion on which to base decisions for each case.
- iii. The Panel's proposal for uninformed monitoring of individuals at low or uncertain increased risk of CJD should be urgently developed (by HPA) and considered (by ethics committee and CMOs) in order to provide this option for other recipients whose implied risk falls close to or clearly below 1%, and for other recipients whose transfusion details are uncertain.

The following further work for the Panel's review prior to its final decision about case no. 1 and other similar cases involving large numbers of donors:

- iv. Development and implementation - after approval - of the Panel's proposal for uninformed monitoring of individuals at low or uncertain increased risk of vCJD. This should enable an option of a) long-term monitoring and enhanced ascertainment of vCJD onset for other recipients who are not considered as 'at-risk' and actively informed of their potential exposure to vCJD, and b) safe-keeping of these individuals' details for notification and/or offering of vCJD testing or treatment in future, if appropriate.
- v. Extension of the risk assessment to look at a range of scenarios for various transmission probabilities, numbers of donors and "thresholds" (1% or otherwise) in order to disentangle the issues involved regarding the risk status of donors and their other recipients, and to guide the Panel in decisions concerning the number of donors to a vCJD case that should be considered as 'low' or 'high' with respect to management of other recipients.
- vi. Further discussion of how the use of a percentage risk threshold for assessing patients to be considered 'at-risk' relates to the balance of public health benefits, for example how the rationale for a threshold may be affected when applied to individuals who are already ineligible to donate blood, and the pros and cons of using the same threshold for everyone regardless.

ACTIONS: HPA/HPS and NBS/SNBTS to implement recommendations (if approved)

DH ESOR to prepare further work for Panel discussion

10. Risk assessments for consideration by the Panel (CJDIP 16/09)

The Panel received an update on risk assessment work from the DH ESOR department.

10.i Revised surgical risk assessment

This version has incorporated new information (notably on tissue infectivity and on decontamination) in order to calculate new estimates of the potential risk of secondary transmission via healthcare instruments. Some new estimates of tissue infectivity were lower than before; estimates regarding the effectiveness of instrument decontamination were more pessimistic than before; and new evidence suggested that material did not have to become detached from instruments in order to transmit vCJD infectivity (ie. the 'contact only' mechanism). Abnormal prion protein is also now known to be extremely thermostable. This means that prolonged contact with tissue adhering to instruments following decontamination can probably transmit infectivity. Animal models suggest that it may take only a few minutes contact with tissue for instruments to pick up infectivity, though rather longer (eg. 30 minutes contact) to transmit infectivity. The implications of the new information have been analysed in the revised risk assessment. In neurosurgery, it is now estimated that infectivity could be carried by instruments through many (up to 52) cycles of use and decontamination. The revised assessment therefore raised the question of an appropriate cut-off for the number of patients on whom neurosurgical instruments were subsequently used who should be considered potentially at-risk for public health purposes. For 'medium' infectious tissues there may be cause to consider a division – with 'medium low' tissues (anterior eye and some peripheral lymphoid) only posing a significant risk (potentially to 1% or greater) to the first subsequent patient. It was reported that vCJD infectivity in tissues was due to be discussed at a World Health Organisation (WHO) meeting the following week. It was therefore decided that the implications of the revised surgical risk assessment for Panel advice would be considered by a technical subgroup once the deliberations at the WHO meeting, and of the next ACDP TSE Working Group meeting, were available. In the meantime, members were invited to comment on the risk assessment provided, and its implications.

ACTION: Secretariat, Panel members

10.ii Bone, organs and tissues

It is clear from these new risk assessments that recipients of bone, organs and tissue from donors found to be infected with vCJD should be considered as at high risk of infection, because of the relatively large volume of material transplanted. (This implies that a high dose could be carried even

by tissues whose specific infectivity lies well below the level of experimental detectability.)

Replacement of the transplanted material may be an option for recipients of implicated bone, organs and tissue. However, there is an issue concerning the traceability of bone that is supplied by a number of organisations, including the UK Blood Services. Information about traceability of transplanted material could be requested from the MSBTO tissue subgroup (next meeting on 22nd September) and this issue would be revisited by the Panel at future meetings.

11. Panel 'framework' regarding tissues and organs (CJDIP 16/10)

The Panel received a paper setting out options for Panel advice concerning the recipients of bone, organs and tissue. It was agreed that a subgroup of the Panel would be invited to consider the proposed framework for this advice in detail.

ACTION: Secretariat

12. Update on decontamination programmes (CJDIP 16/11a,b)

The Panel noted written reports on progress in improving decontamination programmes in England and Northern Ireland. In England, 18 joint ventures were being developed to modernise sterile services in 82 NHS trusts, with a view to being implemented from 2006. The Healthcare Commission has included decontamination in its inspections since April 2005. Work continues on the joint project to develop a guide for the procurement of track and trace, and surgical instrument management systems. In Northern Ireland, the Department of Health, Social Services and Public Safety has established a steering group to oversee the implementation of the 55 recommendations of the Independent Review of Endoscope Decontamination in Northern Ireland.

13. Information update (CJDIP 16/12)

The Panel received an information update from the National CJD Surveillance Unit (NCJDSU). The number of deaths from vCJD in the UK was 150 to date; seven individuals diagnosed with probable vCJD are still alive. There has been an increase in the number of cases outside the UK: 14 cases in France, 3 in Ireland and 1 each in Italy, USA, Canada, Saudi Arabia, Japan, the Netherlands, Portugal and Spain. One case in Ireland and the cases in USA, Canadian and Japanese cases have had a travel connection with the UK (although very short for the Japanese case). All the countries with cases had BSE and also had imported food products from the UK. The overall incidence of

vCJD had declined from its 1999 peak, but there had been more new cases (onsets) in 2004 than in 2003; so far in 2005 there had been over 30 referrals to the NCJDSU.

The Panel noted the items circulated for information.

14. Any other business

A number of Panel members had raised the issue of the impact of patient notifications about risk of vCJD on the quality of life of the individuals concerned. It was suggested that the agenda for the January Panel meeting include a substantial item on these issues, with input from experts in appropriate fields.

ACTION: Secretariat

14. Date of next meeting

Thursday 19th January 2006 from 10.30am to 4pm at BMA House in London.