The European surveillance system for Creutzfeldt-Jakob disease

Prof RG Will and Dr RSG Knight
National CJD Surveillance Unit

A collaboration between countries for the study of all types of Creutzfeldt-Jakob disease (CJD) started in 1993 and has since expanded to include all member states of the European Union. Other countries now involved with this system, designated EUROCPJD, include Argentina, Australia, Canada, Israel, Iceland, Japan, Norway, Switzerland and the United States. The study has been funded by the European Union since it started, (although some countries finance their own involvement with the group) and has been co-ordinated from the National CJD Surveillance unit in Edinburgh, with data analysis centred at Erasmus University in Rotterdam.

The original aim of the project was ‘to compare data on CJD between countries in order to identify any change that might be linked to bovine spongiform encephalopathy (BSE) and the hypothesis in 1996 that variant CJD might be caused by BSE’. It depended to a large extent on data from EUROCPJD, which indicated that, at that time, vCJD was only occurring in the UK. Since then the project has continued to provide comparative data on CJD between countries. The accumulation of data on a very large number of well-documented cases of CJD has led to a large number of publications on the epidemiology, investigation and characteristics of all forms of human prion disease and to the provision of data on CJD on a website: www.eurocjd.ed.ac.uk.

In order to achieve these objectives a number of actions have been essential:

1 Establishing national surveillance systems for CJD in all participating countries.
2 Harmonising methodologies for case identification
3 Creating common criteria for the classification of suspected cases of CJD of all types including sporadic, iatrogenic, genetic (familial) and variant forms.
4 Agreeing on the information on cases to be collected by all centres.
5 Sharing a common questionnaire on potential risk factors for CJD.
6 Centralising anonymised data on cases to allow analysis of trends in the numbers and types of cases per country and to study the overall characteristics of CJD.

These aims have been achieved by all the countries in the system and this has allowed accurate

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**Tonsil testing**

The Health Protection Agency, to assess the spread of vCJD, is to test 100,000 tonsils which have been supplied by hospitals after operations throughout the country since 2003. Gillian Turner, representing the Network, was given a tour of the laboratories at the HPA in Colindale, London and an explanation of the testing to be carried out. Preliminary analysis of the 40,000 pairs of tonsils already in stock is expected in the spring.

**Fourth case of vCJD transmitted by blood**

A fourth case of iatrogenic vCJD, transmitted to a patient nine years after receiving an infected blood transfusion, has been reported by the UK Health Protection Agency (HPA).

The new case is alive and under specialist care. He received blood nine years ago from a person who later was found to have vCJD. The same donor is associated with one of the three previous cases.

Professor Peter Borriello, director of the HPA’s Centre for Infections, said, ‘This new case increases our concern about the risk to the small group of people who had blood transfusions from donors who, unknowingly at the time of donation, must have had vCJD infection’. But he added that precautions had already been taken to reduce the risk of transmitting variant Creutzfeldt-Jakob disease by blood.

A total of 66 people in Britain are known to have received transfusions infected with vCJD. Three of those cases, including the one revealed in January, went on to develop symptoms of the degenerative disorder. A further patient had no symptoms and died through unrelated causes.

**Family support day**

A very successful family support meeting was held on Saturday 11 November 2006 at the Burlington Hotel, Birmingham.

Thirty members of the network, with experience of all strains of CJD including families who had lost loved ones through blood-associated vCJD, attended. They came together to share experiences and to ask those unanswered questions.

We were pleased that, amongst those attending, four women who lost their husbands through sporadic CJD arranged to keep in touch with each other and planned to join up for lunch in the New Year.

Letter received after the meeting:

Just to say how good it was to meet other families to talk to with the same horrific experiences that we have gone through, I wish we had longer time to talk to one another.

Thanks, EB

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**Recent CJD figures**

The number of deaths of definite and probable cases in the UK, up to 2 March 2007. Source: the CJD Surveillance Unit in Edinburgh

<table>
<thead>
<tr>
<th>Year</th>
<th>Sporadic</th>
<th>Iatrogenic</th>
<th>Familial</th>
<th>GSS</th>
<th>vCJD</th>
<th>Total*</th>
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<tr>
<td>2004</td>
<td>51</td>
<td>2</td>
<td>4</td>
<td>1</td>
<td>9</td>
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<td>6</td>
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<td>2006</td>
<td>57</td>
<td>1</td>
<td>6</td>
<td>3</td>
<td>5</td>
<td>72</td>
</tr>
<tr>
<td>2007</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
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Fundraising

2005 case of H-type BSE in a cow

During routine research carried out by the Veterinary Laboratories Agency (VLA), test results have revealed a single case of H-type Bovine Spongiform Encephalopathy (BSE) in the UK in 2005. This form of BSE has already been identified in several other European countries in addition to Japan, Canada and the United States of America.

The cow died on a farm in Dumfries and Galloway at 13 years of age. The carcass was tested for BSE in accordance with EU requirements for testing all fallen stock aged over 24 months. Test results confirmed the presence of BSE. The carcass was incinerated and the offspring from this cow were culled in line with current BSE regulations.

In August 2006 the VLA began a retrospective examination of brain samples taken from previous BSE cases as part of a research programme designed to analyse different types of BSE in the national herd. The aim of the study is to determine whether unusual cases of BSE, had in fact occurred in the UK in the past. The studies are ongoing however this case has been identified as H-type. All forms of BSE are treated identically therefore no additional action would have been required in this case.

The Spongiform Encephalopathy Advisory Committee (SEAC) will examine all the available data on this case during a discussion of different forms of BSE worldwide at their next meeting on 10 May 2007.

Stop press: UK defra report that an atypical form of BSE has been identified in a single cow in the UK in 2005
(Source: Defra information bulletin 9 March 2007 ref 71/07)

MIDLANDS FUN RUN Our grateful thanks to Hugh O’Sullivan and his brother Roger who raised £1200 for the Network, in memory of their father Keith, who died of Sporadic CJD. They ran 8.5 miles in the Midlands Fun Run

In memory

We would like to extend our heartfelt thanks to the friends and families of those listed below for the recent donations received in their memory.

Patricia Selby
Joyce Curtis
Kathleen Marie Bennett
Peter Turner
Geoff Burgess
Rose Elizabeth Smith

Hydro Active Women’s Challenge

On Sunday 3 September Helen Mumford took part in the Hydro Active Women’s Challenge in Hyde Park in memory of her grandmother. Helen says, ‘Late last year my grandmother died of what we and the doctors thought was CJD. After the post-mortem it turned out she died of lymphoma which attacked her brain but didn’t show on any of the scans, but we all lived with what we thought was CJD for the remainder of her life. As a family we know how it feels to live with a family member with CJD and I really wanted to support this network so that they can help other people dealing with the same thing.’ Helen raised £116 in the 5Km challenge run.

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European surveillance system
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information on CJD to be
accumulated, which has been of
critical importance to the response
to the public health challenges
posed by CJD. The diagnostic
criteria for sporadic and variant
CJD have been adopted by the
World Health Organization and by
the European authorities, including
most recently the European
Centre for Disease Prevention
and Control. The EUROCJD
system is responsible for providing
information to the European
authorities on all forms of CJD.

One important question is
whether the frequency of CJD of
different types is the same in all
the countries and the EUROCJD
system has shown that accidentally
transmitted CJD, particularly that
caused by previous treatment with
human growth hormone, occurs
mainly in France and the UK,
while genetic forms of human prion
disease occur most frequently in
Slovakia and Italy, although all
countries have cases of this type.
Variant CJD is primarily a disease
identified in the UK, consistent
with a link with BSE, but cases
have been found in a number
of other countries, notably in
France. The table below shows
the current number of cases of
vCJD worldwide and includes
cases in which exposure to BSE is
thought to have happened while
the individual was living in the UK,
rather than the country in which
the person was living when the
diagnosis was made.

The frequency of sporadic CJD
is very similar between countries
and this is demonstrated in the
graph on page 5, which show the
number of deaths from sporadic
CJD per million population over a
period of years in some of the larger
European countries.

A high rate of sporadic CJD in
Switzerland in recent years is
not understood and whether this
is a chance occurrence remains
uncertain, although the rate of
sporadic CJD in Switzerland has
dropped in the past year to be
more similar to the other countries.
The fact that the overall rates for
sporadic CJD are very similar in all
countries is of great importance. If
there were unusual forms of CJD,
linked to BSE but not recognised
as such, then this should result in
a higher rate of CJD in the UK
in which the human population
were exposed to BSE to a much
greater extent than the other
countries. This has not happened
and study of the characteristics
of the cases such as the age of
patients and the duration of
illness is also very similar between
countries. This argues against the
possibility that there are new and
unrecognised forms of human BSE
infection occurring in the UK,
but it is essential to continue to
collaborate between countries
to ensure that differences in
the characteristics of CJD that
may develop in the future are
not missed. It is only through
the systematic study of CJD and
comparison between countries
that this can be achieved.

Sporadic CJD varies in the way it
affects individual patients and this
is due in part to variations in the
prion protein gene make-up and
the type of abnormal protein that
is deposited in the brain. A study
of over 4,000 case of sporadic CJD
by the EUROCJD group has shown
that there are a number of other
factors that influence how long
individuals live after the disease has
started and this includes gender,
with females living longer and the
age of the person, with younger
people living significantly longer.
For example about 90% of sporadic
cases aged over 75 years die within
a year of the first symptom whereas
about 50% of those aged less than
50 years survive for more than
a year. This work is essential to
assessing any potential treatments
for CJD because the effect of any
treatment must take into account
the variation in survival in patients
even if they have not been treated.

Other subjects of research include
studies of risk factors for the
development of disease and to

<table>
<thead>
<tr>
<th>Country</th>
<th>total number of primary cases (number alive)</th>
<th>total number of secondary cases: blood transfusion (number alive)</th>
<th>cumulative residence in UK &gt; 6 months during period 1980-1996</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>162 (6)</td>
<td>2</td>
<td>164</td>
</tr>
<tr>
<td>France</td>
<td>21 (2)</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>R of Ireland</td>
<td>4 (1)</td>
<td>-</td>
<td>2</td>
</tr>
<tr>
<td>Italy</td>
<td>1 (0)</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>USA</td>
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<td>Canada</td>
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<td>Japan</td>
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<tr>
<td>Netherlands</td>
<td>2 (1)</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>Portugal</td>
<td>1 (1)</td>
<td>-</td>
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</tr>
<tr>
<td>Spain</td>
<td>1 (0)</td>
<td>-</td>
<td>0</td>
</tr>
</tbody>
</table>

*the case from Japan had resided in the UK for 24 days in the period 1980–1996
date there is no good evidence that sporadic CJD is caused by any environmental factor such as past diet, occupation or previous medical or surgical events. This contrasts with a UK study that suggests that variant CJD is caused by past exposure to particular foodstuffs that contained high levels of the BSE agent. Study of the investigations in CJD is a major priority and it was through the EUROCJD system that the 14-3-3 spinal fluid test is now included in the criteria for diagnosis. Currently there is a major effort to assess the usefulness of MRI brain scan in the diagnosis of sporadic CJD. The hope is that the diagnosis of CJD can be improved to allow accurate early diagnosis and this will be of great importance should effective treatments be identified as treatment is only likely to be of benefit if it is started early in the clinical illness.

Thanks

All of us involved in the surveillance system for CJD in Europe are aware that none of this work would be possible without the help of patients and their families and we are all grateful for the extraordinary level of cooperation with this work across Europe and beyond. We believe that the data produced by this work is of primary importance for the protection of public health and also allows important scientific advances that contribute to improving the speed and efficiency of diagnosis of CJD. A continuing objective is to understand why people develop sporadic CJD in the hope that one day this terrible disease can be prevented. To this end we hope to be able to continue to work together the families of patients and to continue to make available, through our website and scientific publications, the information we collect and analyse. One of the lessons from the international study of CJD is that combining data on a rare disease can lead to scientific discoveries that cannot be provided by a single country working alone.

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I lost my Dad to Sporadic CJD on 4 September 2005. He was only 54 years old and a man who was so full of life and fun until this terrible disease took him from us.

I cannot express in words just how difficult it’s been, trying to comprehend what actually happened and why, as well as actually accepting that I will never see him again.

Dad was a fit and healthy man, rode a pedal bike everywhere and was known for his fun personality. On holiday in Portugal in October 2004 we noticed that he appeared not to be his usual self. He had started with a pain in his hip at around this time, and went to see the GP regarding this. As well as this, he had a slight tremor in his bottom lip that was only really noticeable when he was excited about something. By February 2005, the hip pain was intense and he was looking very tired and drawn. He went back to the GP who referred him for an X-ray. Nothing appeared on the X-ray, but the pain was enough to keep him awake at night. He was becoming snappy, started to lose weight and had a general lack of interest. This simply wasn’t like Dad at all.

I had not seen Dad for a few weeks and was shocked when I saw how much weight he had lost and that he was now unsteady on his feet. He appeared to look like he was drunk and held his arm either to the front or back of himself to try and steady his balance. This was heartbreaking to watch, but Dad being Dad just laughed it off. I was so worried about him that I started looking into sending him to a chiropractor as I thought that this would maybe help with the pain, but he would have none of it. We begged him to return to the GP but he said that they couldn’t help. In the end I booked an appointment with his GP and my sister and I took him. He saw a different doctor this time, and my sister and I went in with him and begged them to hurry the neurologist’s appointment. He did, but also sent dad to an orthopedic clinic.

When we got back from the doctor, Dad burst into tears and that’s when we started to think that he thought it was something more serious. I had never seen Dad cry before, and was overcome with emotion. That is when we started looking on the internet into neurological disorders such as MS, Parkinson’s and other conditions. Up until now he had still been working, but being a chef and carrying hot food around, he just couldn’t take the risk and was signed off from work. I remember him telling me he needed to look out for number one and I agreed he should take it easy for a change.

He attended the orthopedic clinic. They were concerned over his lack of balance and co-ordination generally and they put in an urgent referral to the neurologist.

Several weeks passed and his condition worsened. He could not stand for long periods of time, was unsteady on his feet, lacked co-ordination and could not really feel his right arm and leg. His speech was slightly slurred and he appeared to forget things. When he could walk, he veered to one side. He had also been heard falling over. The jerking fits had also started and he appeared not to be able to control his leg at all. The lip tremor appeared to be worse too. It was my brother’s 30th birthday on 13 July, and we had a gathering for him at Mum and Dad’s. Being one of four children we always celebrated together, especially important occasions such as this. The general feeling was that it would not be fair on Dad for us all to go out as he felt conscious of his condition and did not like the attention he felt he would get. He was especially snappy, and stomped off upstairs to get away from the people that were there. We later found out that he had been crying as he felt he could not join in as he would normally do. He cheered up later on and we had a good night in the end, but we knew he was not himself and that something had to be done.

He had been crying as he felt he could not join in as he would normally do.

Dad saw the neurologist on Friday 15 July, and only ten minutes into the appointment, they said he would have to be admitted and needed an urgent MRI scan. So much for the urgent referral – this appointment had taken around six weeks! The urgent MRI scan did not happen until the Monday after, as the hospital appeared to almost shut down at the weekend. Dad was also placed on a cardiac ward as there were no beds on the neurological ward. By now he could not walk, could not sit up straight and the jerking was much worse. We were increasingly concerned and told the staff on the ward. Dad said that he felt that they thought he was going mad and he told them he hadn’t lost his marbles!

The results of the MRI were inconclusive, as was a subsequent CT scan. We felt one neurologist was especially unhelpful and kept trying to get Dad to do things he
simply could not do. The other staff were great, but the neurologists were cold. He then had a lumbar puncture and we were told that he could have cerebellar ataxia. We then forced them to move Dad to the correct ward and when he got there, the first question a nurse asked was ‘Does your Dad eat a lot of meat?’ This set alarm bells ringing and I looked up cerebellar ataxia and found the link to CJD. The doctors still said nothing and Dad was now very frightened and could not eat or drink properly as he could not swallow well. He could barely talk, write, or go to the toilet and had to have a catheter fitted. He was tearful, having hallucinations and the jerking was so bad he nearly fell out of bed so bed guards were fitted. The weight continued to drop off. We were horrified to find out from a staff nurse that he thought that Dad had CJD as he had seen it before and there had been six other cases in the same hospital in the last year or so. The neurologists said they needed a second opinion.

It was here that he had an EEG and a second lumbar puncture. By now Dad appeared sensitive to any fast response or movement, and I felt he had vision problems. He was okay though, if you explained what you were going to do for him – for example, adjust his bed or pillows. He understood everything, which surprised the doctors. He needed palliative care and suction of his mouth and had a feeding tube inserted and complained of pain at the back of his head. He would get frustrated as he tried to communicate, but we got round it with nods, smiles and thumbs up. He was especially upset one morning that two nurses had been talking over him, obviously about his general state of health. I had never seen him so angry before, needless to say the incident was never repeated. Despite things, we still even got lots of laughs. I think this was Dad’s way of making it easier for us to deal with. He was put on Clonazepan for the jerking which calmed him down. Dad never gave up hope and neither did we. The consultant then confirmed our worse fears with a diagnosis of Sporadic CJD, a disease that affects one in a million. My world fell apart.

They explained that the spinal fluid test and the EEG had confirmed this. They explained about CJD and what to expect. Dad was taken back to the local hospital and that is when the Edinburgh team came to question us. They told us he did not have long left. We made a family decision to remove the food tube, but Mum wanted to check this was okay with Dad first. He was practically unconscious but still very aware. This has to be the most difficult conversation that I ever had with my Dad, and one of the last. I asked him if he knew what would happen if the tube was removed and did he agree to this happening. He nodded twice and he agreed that he had had enough of fighting now. We were inconsolable. He was so thin and my heart broke every day that I saw him this way. I was disgusted when the neurologist came to his room just before our talk with Dad to say that they would not resuscitate Dad if he had a cardiac arrest. I was more upset that although he was on morphine, he would have heard what he said. I could have launched at him, but was too shocked really to react. It was something he didn’t need to say. With the help of a fantastic sister on the ward we finally managed to get Dad home. We operated shifts to help Mum and had wonderful community nurses who stayed through the night and assisted with medication. Dad was on oxygen and a morphine syringe driver to ease pain and to generally make his life more comfortable. We were able to take real care of him, cutting his nails and all the personal touches that you can give when someone is in the comfort of their own surroundings. He was comfortable and we all pulled together as a family. We always knew we were close, but realised this even more so now.

An earlier diagnosis of this disease would have given my family and I more time to converse with Dad while he was still able

There were false alarms as Dad’s breathing became more laboured. He fought a long brave fight against this disease and lived an amazing 11 days after all food and drink was removed. He fought so hard not to leave us, but in the end he finally gave in and passed away peacefully, with us all by his side, on 4 September 2005. A mixture of relief and shock was felt by us all.

I would like to state that an earlier diagnosis of this disease would have not changed the outcome, but would have given my family and I more time to converse with Dad while he was still able. I feel that there needs to be more of an awareness of CJD and its symptoms for GPs. This way people could get help more quickly and patients and relatives would suffer a little less.

I still look at my favourite picture of my Dad, smile and cry, still thinking I will see him whizzing around town on his bike, or open the front door when I visit mum. Still in disbelief, still not really comprehending that he is gone, I will never get over it. The one comfort I do have is that I know that as a family we did all that we possibly could and that he knew how much we loved him. I feel him around all of the time; he is never very far away. They say CJD affects one in a million, and he was certainly just that.
In October 2003 my darling husband Deryck died, a wreck of a man lying in a hospital bed surrounded by his family and his little dog. This could have been so different, if only we had had the correct diagnosis, of vCJD.

Deryck had suffered from prostate cancer, and in 1996 he had a radical prostatectomy, during which he was given blood. He bounced back from this setback as only he could do. This man of mine was the eternal optimist, saw the funny side of everything and lived life to the full. He was Santa Claus to the children at Christmas and the teller of wonderful stories at all times. During his years as a Royal Marine his nickname had been Smiley, and that was his natural expression.

During the next six years he had been able to put his cancer behind him and concentrated on teaching himself new skills. Writing for pleasure – what an imagination; the stories he has left us – as well as glass painting, woodcarving, using a lathe, painting with watercolours, and making model soldiers.

Late in 2002 his mood began to change, he seemed to lose his self-confidence, and what was worse his sense of humour. He complained that he had fallen several times when walking our little dog Annie. His hands began to tremble and he would drop things. But most of all he needed to be near me at all times for reassurance. He drove the car for the last time in January of 2003. He took it for a run to charge the battery and got lost on roads that he had known all his life.

I could go on indefinitely about the various symptoms that Deryck experienced, but the point that I am trying to make is that had we been aware of his diagnosis, we could have managed his last months so differently.

Alison, our daughter, was her Dad’s pride and joy, and he would tell anyone that would listen about her achievements. During his final illness she was such a support and continues to be so.

Deryck’s condition deteriorated and he was seen by various doctors. He underwent many tests including MRI scans, lumbar punctures, X-rays, EEG, ultra sounds, blood tests, and psychology profiles. All these proved inconclusive and after different suggestions it was decided that he was suffering from rapid onset dementia. We were told to find a bed in a nursing home, something I had always promised would never happen; but I had not planned on him needing support so quickly and I was still working full time four nights a week. The mortgage had to be paid and we did not have sufficient funds for me to take two years off to look after him – which is the expected duration for this type of dementia. Whilst looking for a home that would be able to cope with my Deryck his consultant changed his mind and informed us that he could stay in hospital.

His condition deteriorated so rapidly that following this decision at the beginning of October, he slipped quietly away on the 24th.

The only reason that Deryck had a post mortem is because both my daughter and I wanted to know why he had died, and it was following this that the truth began to emerge. We were told initially that he had died from Sporadic CJD, and as devastating as this was, we felt we could come to terms with this, a dreadful disease but one for which there is no cause or treatment. Then came a visit from the CJD surveillance unit during which we discovered that in fact my darling Deryck had died from vCJD. Moreover he had almost certainly contracted this from the blood transfusion that he had received over six years before during his operation. So his life-saving operation had inadvertently been the cause of his death.

I dealt with this news by becoming computer literate and researched Not only the loss of a wonderful man, but so many lost opportunities

By Judy Kenny

Had we been aware of his diagnosis, we could have managed his last months so differently
into this dreadful disease. I discovered that the Department of Health had been aware for some years that Deryck, along with others, had received contaminated blood. Not only were they aware, but had made a conscious decision not to inform us. In making this decision they took the advice of the Incidents Panel. This was the most devastating news that I received. Had we been aware of the possibility of vCJD, we could have handled the situation so very differently. Knowing the short duration of this horrendous disease, I could have taken a break from work, and with the help of the compensation and support scheme, have kept Deryck at home. He could have remained in familiar surroundings, with his family, of whom he never showed any fear; unlike the hospital staff, of whom he appeared to be scared.

During the early part of 2003, whilst Deryck was still able to communicate and make decisions, he expressed a desire to go to Ireland on holiday. This was something we had been talking about for some time. I agreed we would go in September when my holiday was booked. With hindsight or with the knowledge which should have been ours; the Irish holiday would have happened whilst he was still able to enjoy it.

I could go on ad infinitum about the lost opportunities. The point I am making is that it is everyone’s right to be in possession of all relevant medical knowledge. I am aware that not everyone will agree with me, that there are people who will say that they would rather not know. But I have been there and know what a difference it would have made.

Editor’s note: Since Deryck’s death, people who are identified to be at a higher risk through secondary transmission such as blood transfusions are now informed.

A family’s experience of iatrogenic CJD

A brief history

By Paul Smith

My wife had Human Growth Hormone (HGH) treatment in her early teens. At the time both she and her parents were told it was completely safe and there was nothing to worry about. Her HGH treatment was halted in 1984/5 on the discovery of some deaths in the US relating to HGH and CJD. She and her parents received a letter from the hospital in the early 1990s informing them of a slight risk but with no real cause for concern.

We got together in April 1994, and married in September 1995. Karen told me she had had HGH treatment and that there was a possibility that CJD may develop. We said we would worry about it if it happened. Towards the end of 2003 Karen was feeling unwell and she said she was not feeling right. This manifested itself as a persistent cough, sore throat and reduced hearing.

This feeling unwell, which she termed ‘feeling wobbly’, continued into early 2004 when she required my support to walk. From the end of April 2004 I would not let her drive. At this time she consulted our GP who diagnosed vertigo. She was given a course of medication which was useless. On two further occasions she saw the GP who continued with sea sickness pills and vertigo treatment. I went with her on 3 June 2004, and informed the GP in no uncertain terms that this was not vertigo. At this time he looked at the back of her eye and at her gait. At this point was the first mention of CJD.

She was seen by neurologists in June 2004, who confirmed a diagnosis of iatrogenic CJD. Karen agreed in July 2004 to undergo therapy with pentosan polysulphate. This required the insertion of a shunt pump into her abdomen, and a catheter into a water ventricle in the brain. Narrow tubing up through the abdomen connected the two.

Karen had regular pump refills but continued to deteriorate over forthcoming months and she passed away on 5 August 2006, approximately 32 months after onset of the symptoms.

Editor’s note: Paul has written some thoughts and information which he found helpful whilst caring for Karen. Due to shortage of space in the newsletter this is not included. If you would like a copy of this it can be obtained from Gillian Turner at the CJD Support Network office.
I was one of the 300 women who heard on 1 September 1993 that we could have been infected with CJD when we received pituitary gonadotrophins in the late 60s and early 70s. You may be wondering why I was possibly the only one not shocked by this early morning news item. In the early part of 1992 I had seen a news item about the children who developed CJD as a result of growth hormone injections. Since I had been alerted to my treatment of 20 years earlier warning bells started ringing. I consulted my GP and soon it was confirmed that I had received three injections of pituitary gonadotrophins. I am not an irrational person but this news made me very frightened. My GP has since said that I self-counselled, which I took as a big compliment.

So the news item was not a surprise but I was shocked at the insensitive TV reporting. All I could think about was of the women who were hearing this for the first time. The reference to CJD as mad cow disease deeply offended me and I couldn’t begin to imagine how the other women must now be feeling, not only by the news but by the totally inappropriate reference to cows and madness. I was so cross that I rang up the solicitor who was dealing with the press at our home, my husband and I went to the solicitor who was dealing with these matters for advice about a directive from within. 

All I could think about was of the women who were hearing this for the first time

statement we had prepared for the reporters. Incidentally we later followed up with letters to major newspapers inviting them to seek an alternative to using this dreadful expression and not to underestimate the publics’ capacity to cope with correct medical terminology. We only had one positive response.

Exposure to the media is one thing but my shock 18 months earlier in 1992 was something I took some time to adjust to. I became preoccupied with the notion that in spite of being a person who felt guilty to take an aspirin I had through no fault of my own been subjected to medication that could have been contaminated. This did make me look at life and I made some rather bizarre decisions. I cashed in all my insurance policies and bought a car and visited my parents 200 miles away. I also decided to see the flowers in Turkey on my birthday (6 May). To this day I don’t know how I did this or why I choose such a remote place, but the decision was taken with the support of my family. I was able to take unpaid leave. My students were understanding in spite of not knowing the reasons. I still cannot believe my good luck.

To be able to write this I am obviously still here some 30 years later. It does still hang over me but my out-of-character assertive actions have paved the way to a fruitful retirement when I have devoted as much time as I have been able on researching the flora of a small remote rural village in SW Turkey. Here I rent a room with a Turkish family; I eat with them and have become accepted by the community. At first it was difficult for them to understand what I was trying to do so much so that I was for a while known as the crazy wild flower lady. However my status has improved as they have got to know my family and my dedication to the task. I should at this point make it clear about what I was endeavouring to do. I visited in 1992 and was amazed at the variety of plants in such a small area. I realized that such rich variety may well not continue to exist with the onslaught of tourism. So I set myself the task of seeking to identify and photograph all species of plant. Many exciting aspects of botany have emerged; endemic and ethno botanic plants. The latter group because I have observed at first hand the way my landlady uses plants on a day to day basis in the same way as her forebears.

My involvement in the project has taken my mind off myself and given me a purpose. It has required me to learn some Turkish, computer and camera skills, and most of all to decode the botanical language of PH Davis’ definitive Flora of Turkey. Respected academics in the UK and in Turkey have all been very encouraging and have even found my work useful as I am the only person looking at this small area in detail. I was very pleased to be asked to attend the VIth Plant Life of SW Asia Symposium at Yuzuncu Yil University at Van in Eastern Turkey.

Our life as a family has become richer as a result of the strange decision I made in 1992. The work on the project has enabled me to find fulfillment after being at my lowest. While I do not advocate bizarre behaviour, the Worried Well may sometimes need a very personal directive from within.
Decade past, decade to come

Decade past, decade to come, was a highly successful conference hosted by the CJD Support Network in 2006. Recognised world experts on CJD gave their views and thoughts on the last decade and identified challenges of the future.

In response to requests from members we have included summaries of four of the speakers’ talks. A DVD of the conference can be purchased from Gillian Turner.

CJD: epidemiology and risk factors

Richard Knight
National CJD Surveillance Unit

The UK National CJD Surveillance Unit was established in 1990 and variant CJD was first described in 1996, ten years ago.

Surveillance and epidemiological methods identify the incidence/prevalence of disease, its basic characteristics and attempt to identify risk factors and cause.

The prion protein is central to human prion diseases and it is, therefore, not surprising that the relevant gene (PRNP) has an important role to play, not only in genetic forms of illness. An important polymorphism at codon 129 has significant effects on susceptibility, incubation period (in acquired forms) and even in the resultant clinico-pathological features.

Mortality rates of sporadic CJD (sCJD) have increased in the UK, since 1985, probably reflecting better case ascertainment and advances in diagnosis. However, in recent times, these rates have been significantly below many other European countries; the cause of this is unclear. Current theories of causation favour a ‘spontaneous degenerative’ cause. Given this, one would expect a consistently increasing incidence with age, but there is a decline in the very old; this may reflect under-ascertainment in the elderly. Case-control studies have generally failed to identify any consistent risk factors, but two recent studies have implicated previous surgery.

Variant CJD (vCJD) is thought to be due to BSE contamination of diet. There is no absolute proof of this theory, but a recent case-control study provided some modest support for this view. The relative youth of affected individuals is notable, as is the fact that the age at onset of illness has not changed over the period of the epidemic. All clinical cases to date have been PRNP-129 MM, but there are good reasons for thinking that other genotypes will be affected. Currently, there is a decline in cases in the UK, but there may well be further ‘waves’ due to other factors (for example, in other 129 genotypes). A recent appendix study produced results that potentially increase concern over future numbers. There is a clear pre-clinical phase in human BSE infection, but it is not known
if genuinely subclinical infection occurs.

Iatrogenic CJD (iCJD) has, in the past been due mainly to human growth hormone and human dura mater grafts, presumably from tissue donors with sCJD. However, much recent concern has centred on the possibility of secondary transmission of vCJD, especially by blood. There are now three identified instances of BSE infection being transmitted from person to person by blood transfusion.

During the late 1990s the blood services instituted a number of precautionary measures designed to reduce the risk of vCJD through blood transfusion. While many countries introduced restrictions on blood donors who had resided in the UK during the relevant time period, this option was clearly not available in the UK! But a number of initiatives were introduced, following an extensive risk assessment exercise conducted on behalf of the Department of Health. These included leucodepletion (the removal of white cells from blood), stopping the use of UK plasma for fractionated plasma products, and obtaining supplies of fresh frozen plasma (FFP) for children from non-UK sources.

Further precautions introduced in the last five years have included measures to exclude donors who could be at increased risk of vCJD, for example those who have themselves received blood transfusions, in order to prevent any expansion of vCJD in the population through this route. Careful and sympathetic communication of these decisions to the affected donors has been a major challenge.

At present the epidemiological study continues to generate information which is of importance in helping to delineate the extent of risk through blood transfusion and to identify both blood donors and blood recipients for whom public health measures to reduce any possible risk to others are appropriate. Much work is directed at the future, with active development by commercial companies of both filters designed to remove prions from blood and possible blood screening tests. The blood services are actively engaged in both these major activities, which will undoubtedly come at a cost, and making plans for the introduction of one or both. The impact of both initiatives is likely to be enormous and the major challenge of a blood screening test and its implications on blood donors should not be underestimated.

Much has happened in the last 10 years in relation to vCJD and blood transfusion. The next 10 years are expected to produce major benefit in relation to the risk associated with blood transfusion but the costs in both financial and human terms could be enormous.

What are prion diseases?
Fundamental principles and approaches to developing an effective treatment

Prion diseases are a group of degenerative brain diseases which affect both humans and animals and are also known as the transmissible spongiform encephalopathies. Animal prion diseases include scrapie, a naturally occurring
disease affecting sheep and goats, which has been recognised for over 200 years and is present in many countries worldwide, and the much more recently recognised bovine spongiform encephalopathy (BSE) amongst cattle. The human prion diseases have been traditionally classified into Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler syndrome (GSS) and kuru. These diseases are transmissible experimentally both within and between mammalian species by inoculation with infected tissues and sometimes by dietary exposure. The transmissible agents, or prions, are composed principally of abnormal forms of one of the body’s own proteins, the prion protein (PrP). Prions propagate themselves by recruiting normal cellular PrP into the disease-specific form and this involves a change in 3D shape (protein conformation) and aggregation (many single PrP molecules now sticking together). According to the ‘protein-only’ hypothesis, an abnormal PrP isoform is the principal, and possibly the sole, constituent of the transmissible agent or prion. Interestingly, other degenerative brain diseases for example Alzheimer’s disease, are also associated with accumulation on the brain of aggregates of misfolded proteins.

The human prion diseases have been classified into three aetiological categories: sporadic, acquired and inherited. Sporadic CJD occurs in all countries, apparently striking at random, and affecting 1-2 per million of the population each year. Acquired prion diseases – where the patient has been infected by prions from the environment – include iatrogenic CJD, kuru and variant CJD, and arise from accidental exposure to human prions through medical or surgical procedures, participation in cannibalistic feasts and exposure to BSE prions respectively. Prion infections in humans are associated with long incubation periods during which the individual is healthy; indeed incubation periods exceeding half a century have been documented in kuru. Prion diseases may also be passed from generation to generation in families by a faulty gene. Such inherited prion disease accounts for around 15% of human prion disease and is caused by mutations in the PrP gene, of which over 30 different types are recognised.

Remarkably for an infectious agent that appears to lack its own genome, prions occur in various different strains which produce different patterns of disease or phenotypes. Recent studies suggest that there is not simply a single abnormal disease-associated form of PrP, but multiple different forms with different conformations and differences in their glycosylation (the attachment of sugar molecules). The ability of a protein to encode information in this way has important biological and evolutionary implications.

The appearance of variant CJD, and the clear evidence that it is caused by exposure to BSE, highlighted the need to understand the fundamental molecular basis of prion propagation and pathology and the so called ‘species barriers’, limiting transmission from animals to humans. It is probable that a significant fraction of the UK population, and to a lesser degree other populations, have been exposed to BSE prions. While the number of clinically recognised cases of this fatal neurodegenerative disease thankfully remains relatively small, the number of infected individuals and the eventual epidemic size remain unknown. It is likely that genetic factors will play a key part in determining incubation periods in different individuals. The risk of secondary (patient to patient) transmission via medical and surgical procedures is also unclear at present.

Laboratory mice in which the PrP gene has been ‘knocked out’ – so that they do not produce PrP – are essentially normal, but cannot make prions or develop disease when inoculated with prions. Remarkably, when PrP is knocked out from brain cells during established infection of the brain, onset of clinical disease is entirely prevented and the pathology in the brain recovers. This happens despite the continued accumulation of abnormal PrP and prions to high levels. It appears that normal PrP, rather than abnormal PrP, is the rational target for drugs and a major study is underway at the MRC Unit to develop such drugs. At the request of the UK Department of Health, a protocol and infrastructure for the clinical evaluation of therapeutics has been established: the MRC PRION-1 trial. The protocol was prepared in discussion with UK patient groups and modified in the light of pilot studies. The drug Quinacrine is currently under evaluation. Other candidate drugs which might undergo trial in the future are evaluated by the New Therapies Scrutiny Group.

(c) J.Collinge 20 March 2006, CJD Support Network – Abstract from ‘Decade past, decade to come’, an International CJD Conference

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continued…
A Decade of Pathological Discovery in CJD

Professor James W Ironside
National CJD Surveillance Unit

Pathology has played a key role in the identification and understanding of transmissible spongiform encephalopathies or prion diseases in animals and in man.

Pathological examination of the brain is required to confirm the diagnosis of a human prion disease, but the role of pathology goes far beyond diagnostic confirmation, important though that is. Pathological studies have for many years established the range of diversity in human prion diseases, in terms of the variability in distribution and nature of the brain lesions in sporadic and familial prion diseases. More recently, the major factors influencing this diversity have been investigated, particularly the key role of the prion protein gene polymorphism at codon 129 and the isotype of the abnormal prion protein in the brain in sporadic CJD.

Pathology is a key component of surveillance for human prion diseases, and played an important role in the early identification of variant CJD in the UK. In addition to detailed pathological studies of the brain in human prion diseases, the importance of studying organs and tissues outside the central nervous system has not been overlooked. Studies of the tonsil and other lymphoid tissues in variant CJD allowed the detection of the abnormal form of the prion protein. This key feature of variant CJD has been utilised in tonsil biopsy to aid clinical diagnosis in some patients, and has been used to help estimate the prevalence of variant CJD infection in the UK in a retrospective study of large numbers of tonsil and appendix specimens.

The increasing sensitivity of tissue-based assays for abnormal prion protein has recently allowed its detection in skeletal muscle and spleen samples in sporadic CJD and in skeletal muscle samples in iatrogenic CJD. The development of the PET blot technique suggests that in skeletal muscle; most of the abnormal PrP may be in nerve fibres running in the muscle bundles. The results of these studies not only allow us a better understanding of these diseases and the routes of spread of infectivity, but also provide important information for risk assessments for infection control purposes.

The study of human tissues will continue provide the most relevant information on human prion diseases, more so than from animal models; this is particularly important when the effects of any form of therapy are considered. However, access to and use of human tissues for diagnosis, teaching and research is dependent on the consent of relatives of patients with all forms of human prion disease, to whom my colleagues and I are most grateful for their generosity and support both over the past decade and for the years to come.

Therapy for TSE: a hard look at the current scene

Paul Brown, MD
Bethesda, Maryland, USA

The outbreaks of both BSE and vCJD are waning, but cases continue to occur from infections contracted in the early 1990’s, and secondary transmissions resulting from blood transfusions have recently been identified in 3 individuals living in the UK.

Efforts to detect infection before the onset of symptomatic disease go hand-in-hand with efforts to discover some form of meaningful therapeutic intervention. Several pre-clinical blood screening tests are in various stages of evolution and will probably become available within the next year or two.

Therapy is being directed towards both prevention and cure, with some interesting hints of progress, but it is still not possible to predict when the goal of truly effective therapy will be reached. The good news is that therapeutic studies, which have for so many years lain dormant, are now the object of increasing activity in both the academic and commercial worlds, and that kind of cooperative interest almost always leads to eventual success.

(c) P.Brown, 20/03/06, CJD Support Network – Abstract from ‘Decade past, decade to come’, an International CJD Conference
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Can you help us?

The CJD Support Network is a relatively small organisation and it is very difficult for us to get sufficient exposure to the public in order to raise enough funds to carry out the work we would like to do and which we feel is needed. Each year, attracting public donations gets more difficult as we compete with much larger charities and more high profile causes.

We have been successful in attracting, a three year Section 64 grant for 2006-2009 from the Department of Health. Whilst we are very grateful for this support it only accounts for 40% of our required funding. This grant ensures the continuity of the practical and emotional support that we offer on our 24 hour CJD helpline, and funds our administration costs. However, each year we need to supplement the money we receive and identify other funding to enable us to fund new initiatives, develop our work as needed, fund family support meetings and provide care grants to families who are in financial difficulty through caring for a loved one with CJD.

We are also very conscious that whilst we have been very successful in receiving Department of Health funding for a good many years, we cannot expect this to continue infinitum. We do need to identify other sustainable income streams.

We are very grateful for the support we have received over the years from many of you and much needed money has been raised in a variety of ways:
- In memoriam
- Bequests
- Gift aid
- Public donations
- Sponsored marathons
- Sponsored bike rides
- Sponsored parachute jumps
- Organised coffee mornings
- Bring and buy sales
- And many more....

If you would be interested in helping us or have had experience of raising much needed funds we would be very pleased to hear from you.

If you or a member of your family is interested in doing a sponsored event for us, we can offer CJD tee-shirts, balloons, pens and sponsorship forms to help.

We have joined the Golden Bond scheme of the London Marathon which will guarantee us a place within the next three years. Sadly we have not been awarded one for this year.

We do hope to organise one big fundraising event next year, probably in London. If you feel that you could help us in this or in any other way, or you have contacts that you could introduce us to, we would be very grateful. Please contact Gillian Turner on 01630673993.

Stop Press

We are pleased to announce that the CJD Support Network is funding a three year research scholarship to a researcher at the MRC Prion Unit. The research will be under the guidance and management of Professor John Collinge.

Details about this research on Sporadic CJD will be featured in our next newsletter and on our website. A presentation will be given by the researcher at a future family support meeting.

We would like to offer our grateful thanks for all the donations in memoriam that have been given for research to the network and which have enabled us to fund the first of the three years of this scholarship.

CJD Support Network membership

Becoming a member of the CJD Support Network adds to our strength and enables you to take a full part in the decision-making process and the work of the Network.

☐ I would like to become a member and receive the CJD Support Network newsletter.
☐ I would like to become a member but not receive the CJD Support Network newsletter.

There is no fixed subscription, but you may wish to make a small donation to cover the cost of production and postage of our newsletter: ☐ £8 ☐ £12 ☐ £25 ☐ £50 ☐ Other ______

Please make cheques payable to CJD Support Network

However, if you are a carer and would appreciate free membership, please tick the box ☐

Name ____________________________ Title ____________________________

Address ____________________________________________ Postcode ____________

Telephone ____________________________ Email ____________________________

I am caring for someone with CJD: ☐ at home ☐ in residential care

I am: ☐ a concerned relative/friend ☐ former carer ☐ professional ☐ interested

APR04
Chairman’s letter

Welcome to another CJD Support Network newsletter! Myself and the Executive Committee are extremely grateful for your continuing support of the organisation. It seems hard to think that it has now been an independent charity for over three years and although we have had our ups and downs in terms of our finances the organisation is extremely strong, providing support to many individuals who are affected by CJD or the worry of CJD. Although there have been some noticeable highlights of the last 12 months including our conference last year, the Network is at its best when organising family days. The AGM in November in Birmingham was a highly informative and moving occasion for all who attended.

This letter is a brief opportunity to officially thank Gillian Turner and so many of the other members of the committee who have given their time so freely. I particularly wish to single out our treasurer for all his expertise in the running of the finances. To many of you who have participated in fund raising activities we are also extremely grateful and I wish to send out a big and cheery thank you.

The organisation is of course yours and not anybody else’s and therefore your thoughts and views on matters and reaction to the articles in this newsletter are extremely important. We still do really need to hear from you about important things that are not available or that are not happening. We plan to launch later on in the year a web-based audio tape which will be an information booklet about CJD. We have also refreshed some of our other information booklets to make sure that they are up to date.

If you would like to get involved in any activities then please do not hesitate to contact Gillian or myself.

With best wishes, Angus Kennedy

CJD Support Network Management Committee 2006-07

Dr Angus Kennedy – Chairman
Consultant Neurologist

Maria Bryne – Secretary
Maria is a mother with three children whose husband Graham died with GSS

Mike Curtis – Treasurer
Mike, a former bank employee whose wife, Joyce, recently died of sporadic CJD

John Gilbert – Assistant Treasurer
John’s brother in law died of sporadic CJD

Stuart Durkin
Stuart’s father died of sporadic CJD in August 2003. Stuart is a freelance social researcher

Anita Tipping
Anita is a state registered nurse, RSCN, whose son David died of CJD through growth hormone injections

Michael Bradley
Michael’s mother died of sporadic CJD

Jean Lightband
Jean Lightband is a retired neurological specialist nurse. Her last position was at the National Hospital for Neurology and Neurosurgery

Roger Tomkins
Roger’s daughter Clare, died of vCJD

Sarah Tomkins
Sarah’s husband Edward died of sporadic CJD

Derrick Biggs
Derrick Biggs is our social services adviser and an operations manager with Cambridgeshire Social Services. He is the Association of Directors of Social Services link person for CJD

Dr Andrew Smith
Dr Andrew Smith is a Senior Lecturer in Microbiology at Glasgow Dental School

Judy Kenny
Judy’s husband, Deryck, was the first person to die of vCJD through a blood transfusion. Judy is a retired nurse

Gillian Turner – CJD Support Network co-ordinator