

## Update on variant CJD

Professor Simon Mead  
National Prion Clinic

Last year the National Prion Clinic diagnosed a patient with variant Creutzfeldt-Jakob disease (CJD) at post-mortem examination. All cases of human prion disease are tragedies for their families, but this case was particularly special because the patient carried a common genetic change that had been thought to protect against the disease. Here we discuss some of the background to and implications of this finding.

Prions are lethal human pathogens made from chains of an abnormally folded protein called prion protein (or PrP). PrP is normally found on the surface of cells in the brain, on immune cells and to a lesser extent, elsewhere in the body. Prions grow by the conversion of normal PrP into abnormal or 'rogue' forms. Prion infection can be spread by ingestion of material infected by prions, or through certain contaminated medical or surgical procedures.

Bovine spongiform encephalopathy (BSE) is a notorious prion disease of cattle which became an epidemic in the UK more than 20 years ago. It spread to humans as a new form of CJD called 'variant CJD' and resulted in a health crisis. BSE has been controlled by several measures including the prohibition of feeding animal-derived food products to cattle. The human form of BSE, variant CJD, typically affects younger adults in the UK, and thankfully has been in decline since 2000. Worldwide there have been at least 220 deaths from variant CJD.

PrP contains 253 amino-acid building blocks that are encoded by the prion protein gene; everyone has two copies of this gene and thus produce two types of the PrP. There are different variations in the gene allowing the body to make different types of PrP. Commonly, in the healthy population, there are those who make PrP with a methionine amino-acid at position 129, those with valine only, or most commonly, those with a combination both methionine and valine. We know that these types are important in determining whether someone is more or less likely to develop CJD. In fact, until 2016, all patients with a certain diagnosis of variant CJD made only the methionine form of PrP. Until this new patient was diagnosed, we had wondered if those with other PrP types were completely resistant to the disease. The new patient made both methionine and valine, which is the most common type in the population.

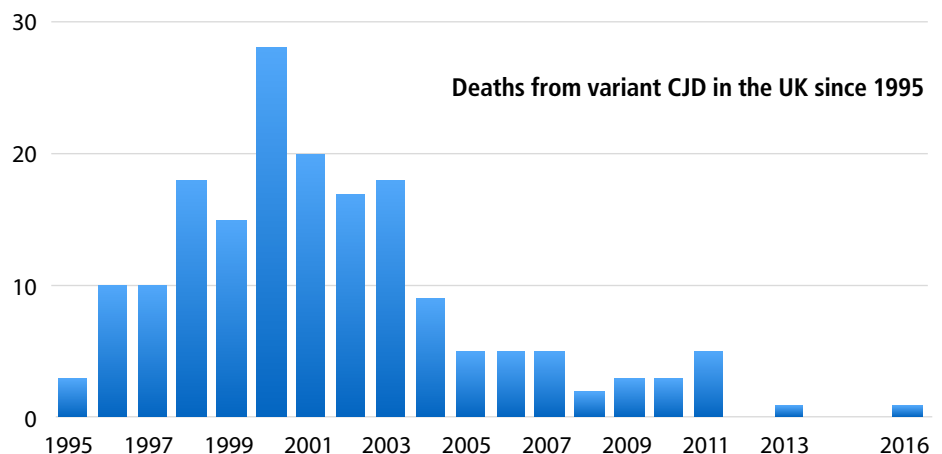
Because our patient was the first with variant CJD and this particular type of PrP we were interested to see if the illness had similar features

compared with previous cases. In many ways, the clinical features were similar, including the age at the start of symptoms, with low mood and balance problems. The brain scan however was different, as it looked the same as seen in the most common form of human prion disease, sporadic CJD. In other words, tests that we did to reach the correct diagnosis were in fact misleading.

Of course, we hope that we will not see any more patients with variant CJD; however, experience of other human outbreaks, like 'kuru', a disease that affected people living in Papua New Guinea, suggests that there may be different waves of cases linked to different types of PrP. We need to be alert to these new cases occurring in patients with unusual and potentially misleading symptoms, signs and test results.

We are very grateful to the patient and his family for their participation in research studies without which an accurate diagnosis might not have been made.

*For further information on this article please go to: [www.nejm.org/doi/full/10.1056/NEJMc1610003](http://www.nejm.org/doi/full/10.1056/NEJMc1610003)*



# Reports from the Annual Family Support Meeting in Birmingham · November 2016



## What is Prion Disease?

**A report on the presentation by Professor Richard Knight  
Consultant Neurologist and Director of the National CJD Research and  
Surveillance Unit**

### Prion disease

Prof Knight started by presenting some basic biology of the human body. The human body is made up of assembled organs that serve specific vital functions, including the brain. Many (but not all) normal brain functions are localized in specific parts of the brain. An organ is made up of small units called cells and proteins are made within the cells.

A gene is a string of code. The code is translated in a chain of amino acids that then form proteins. Mistakes can occur in a string of code that may then affect the structure and function of the relevant protein.

Prion disease involves an abnormality in a specific protein

which undergoes a change in conformation. An individual develops symptoms because neurons malfunction and prion disease is progressive. It is a rare disease with one to two deaths per million people.

The sporadic form occurs randomly in a population, while the acquired prion disease like kuru, iatrogenic and variant CJD result respectively from: cannibalism, surgery or certain hormone treatments, diet and infected blood transfusion. Genetic CJD is inherited due to an autosomal dominant defective gene.

Absolutely certain diagnosis requires neuropathology ie. biopsy or autopsy examination of the brain.

### Clinical diagnosis

Onset is often non-specific. Suggestive clinical picture with the exclusion of other diseases is vital before any diagnosis can be made. Atypical prion disease is hard to diagnose.

Non-specific tests include EEG, brain MRI and the CSF 14-3-3 test.

Specific tests include genetic testing, CSF RT-QuiC, tonsil biopsy for variant CJD and more recently nasal brushing, skin biopsy and blood test. RT-QuiC works well with sporadic CJD but not with variant CJD.

Any diagnostic test needs to be robust and needs careful assessment in practice before routine clinical use.

CJD Support Network invites you to the  
**Annual Family Support Meeting**  
Saturday 18 November 2017 · Birmingham

The 2017 Annual Family Support Meeting and AGM will be held on Saturday 18 November from 10am until 4pm at the Burlington Hotel, New Street, Birmingham.

We do hope you will join us. Each year, families report to us how helpful they have found meeting other families and

being able to ask those unanswered questions from the CJD experts who attend the day.

If you would like further information, or are interested in attending, please phone the helpline on 0800 0853527 or email [support@cjdsupport.net](mailto:support@cjdsupport.net)



# Developing treatments for CJD

**A report on the presentation by Professor Simon Mead, National Prion Clinic**

CJD is a rare form of neurodegenerative disease associated with a change in shape of one of the body's normal proteins, called the prion protein, into an abnormal form that damages nerve cells. Whilst none of the neurodegenerative diseases are currently treatable, in that the progression of the disease can be halted or slowed, there is some optimism that our increased understanding of the basic science of these conditions is taking us closer to future treatments.

## Treatment strategies

Professor Mead spoke about the different strategies that are being taken in the laboratory to develop treatments, including for example, (1) a drug that stops the production of the normal form of prion protein, as we know this can be done in animals without major consequences, (2) identify particular types of the abnormal prion protein that are toxic to nerve cells and find a drug that reduces their formation or prevents their damaging effects, (3) identify drugs that bind to the normal prion protein and prevent it from changing shape into the abnormal form, (4) work out how abnormal prion proteins are toxic to nerve cells and interfere with this mechanism.

## Clinical trial strategies

The discovery of potential drugs then leads to a question about how to prove whether it has an effect in patients. Traditionally this is done with a clinical study called a 'randomized double-

blind placebo-controlled trial'. This means that patients are given either the experimental treatment or a dummy pill, and often, the chances are equal for either option. Neither the doctor nor the patient knows which has been given. The patient with CJD would then be followed up, possibly for the rest of their life on the trial treatment. At the end of the trial it is revealed who was taking the experimental treatment and who the dummy pill, and their outcomes compared statistically.

The advantage of the randomized controlled trial is that it avoids sources of bias that can lead to the incorrect conclusions being made. The disadvantage is that a patient may only receive a dummy pill and so may not want to participate. This problem is often found when the drug is available for prescription for other conditions, and patients might be able to access treatment outside of the study. In CJD the short clinical duration of the disease mean that patients might only have one chance to try an experimental treatment.

An alternative is an 'observational study'. In this circumstance all patients are treated with the drug and both the doctor and patient know what is being prescribed. Whilst this is more attractive to patients, it is harder to tell if the drug and treatment has really worked because of sources of bias.

There have been five drugs already tested in prion disease

trials (of observational and randomized types) and there is no compelling evidence that any had an effect.

## Difficulties with trials in prion disease

There are some major challenges of clinical trials in prion disease:

- It is a rare disease and it is rapidly progressive.
- There are no (until recently) established measurements to decide if treatment is working.
- There is little commercial interest in drug development.
- It is hard to recruit participants to enlist in placebo controlled trials.

## Advantages of trials in prion disease

There are also some advantages that might accelerate the discovery of treatments:

- Patients have little to lose as no-one recovers from the disease. This might encourage people to want to try experimental treatment.
- There are excellent laboratory 'models' of how the disease works, and therefore how drugs might be developed.
- Prion diseases attract funding for academic research because of great interest in the basic biology of the disease
- The National Prion Monitoring Cohort study and others have led to the development of measurements and trial methods that should make clinical trials more reliable in the future.
- There is an increasing focus on dementia and other neurodegenerative diseases in general, which includes the possibility of a drug that might work in multiple diseases.

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### **PRN100 – one possible experimental treatment in the future**

Professor Mead went on to talk about the development of a vaccine type treatment. At the MRC Prion Unit and elsewhere around the world researchers have conducted long-term research to investigate potential antibody treatments for prion disease and to see if such treatments might work and what side effects or other safety issues might be anticipated.

The immune system recognizes foreign proteins and other parts of germs as being alien to the body and this leads to the body producing specific antibodies tailored to fight that infection. However, since prions are formed from one of the body's own proteins they are not recognized in the same way by the immune system and lifesaving antibodies are not produced. This is one of the reasons why prions are so lethal.

PRN100 is an antibody specifically designed to bind tightly to the normal protein with the aim of preventing it from combining with the prions and in this way stop a chain reaction and formation of new prions.

Antibodies have also been found to have potent activity in laboratory test models of prion disease.

Laboratory tests have provided a 'proof of principle' that PRN100 works by preventing the chain reaction and the formation of new prions, but there are still many challenges for patient treatment. Despite these unknowns, given the lack of any alternative treatment for a disease that is rapid and invariably fatal, the research team at the MRC Prion Unit, as well as patients, relatives and colleagues at University College London Hospital feel that PRN100 should be offered to patients with rapidly progressing

CJD at this time. The researchers are seeking Trust approval to do this. More details can be found at [www.cureCJD.org](http://www.cureCJD.org)

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*The family members at the meeting were encouraged in learning of the proposed treatment and wished Professor Mead and his team success in their work. A family member, recently bereaved, said they were sad at hearing of a possible experimental treatment having just lost a loved one to the disease.*

*Professor Mead raised a precautionary note, saying that it is very 'early days' in our journey to develop a treatment, and that most drugs fail in clinical trials, but he was also optimistic that our increased understanding of the disease will lead to a treatment at some point in the future.*

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## **Round table discussions**

### **Some of the issues raised and discussed in breakout groups**

1 Members were horrified that 'mad cow disease' is still used to refer to patients with CJD.

2 A member felt the care accorded to their loved one by funeral personnel was lacking. We were told that undertakers have their own guidelines to follow.

3 A member spoke about the failure of the consultant to show up on their agreed appointment – instead it was their secretary who turned up asking the family to sign the form 'for tissue research', to which they did not agree. The family subsequently received help from the Surveillance Unit in completing the form.

4 One concerned member seems to find it hard in herself to accept the post mortem analysis result from the Surveillance Unit.

5 A member asked how to go about having a genetic test. It was explained that tissues need to be preserved correctly. She also pointed out difficulty among family members who want to be tested and those who don't. The concerned member did not want to know the result, if it happened to be positive.

6 Members reported that support for carers by their employers is lacking. Only one or two in the group said they had the full support of their employers.

### **Attracting families**

Prof Knight asked the audience for any ideas to make the annual family support meeting and AGM more family friendly. A social dinner for all attendees either the night before or on the evening of the event was mentioned. Members were asked for feedback.

We would be pleased to receive your thoughts about extending the annual family support meeting to two days. The American and Australian CJD support groups have a two day family support meeting and this has proved very successful.

## Our journeys

### Roger and Sarah Tomkins spoke about their personal journeys with CJD

Roger Tomkins was involved when his youngest daughter, Claire, aged 23, was admitted to hospital. Following several clinical tests and observations, Roger was informed that his daughter needed to be sectioned due to her depression. The neurologist caring for his daughter informed Roger and his wife that he had been in touch with the Surveillance Unit in Edinburgh and the family was informed that their daughter had vCJD. Their daughter had been a vegetarian for 11 years. Mr Tomkins and his wife decided to take their daughter home and care for her themselves. This was the catalyst for Roger to get involved with CJDSN. He was an active member of the BSE inquiry and, until this meeting, he was the

CJDSN conduit to the Human BSE Foundation.

Claire's care lasted for nine months until she passed away. At the same time, Roger's wife was diagnosed with an ovarian cancer and she sadly passed away few months after their daughter. Roger retired shortly after losing his wife.

Sarah Tomkins was an economist for Hoover Appliances and her husband an artist.

Sarah picked up signs that something was wrong with her husband, when she saw that the work he was painting had two heads. She rang and spoke to her GP who contacted the Surveillance Unit in Edinburgh. Her husband was diagnosed

with sporadic CJD. With support from her GP, Sarah cared for her husband at home. He passed away within a month. Sarah joined the CJDSN in 1999.

Roger and Sarah met when Sarah was having a dinner party and Roger was an invited guest. They have been married for 13 years. They both give talks about CJD. They run their own business and remain busy fundraising for the Network and other worthy causes.

Roger and Sarah have decided to step down from their work with the CJDSN committee.

Though it is sad to say goodbye to them, Sarah and Roger have shown that there is life after CJD.

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*Ed: We are very sorry to see Roger and Sarah step down from the CJD Support Network committee. They have been very helpful and supportive to the work of the CJD Support Network and they will be sadly missed. At the Family Support Meeting, we thanked them for their support and wished them a happy and healthy 'retirement'.*

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## APPRECIATION

### Graham Blades

#### A founding member of the CJD Support Network

by Gillian Turner

On my first day with the CJD Support Network, I was told that if I wanted to know anything about CJD, ring Graham Blades.

Graham's wife Janet had been diagnosed with CJD in 1988 at the age of 27, and given 12-month's life expectancy. They had two young children and Graham decided that Janet would be cared for at home. At first, they were able to obtain the services of a private nurse, but In 1994 Graham decided to leave his job to care for Janet himself.

In 1992 Graham, and Bob Will from the National CJD Research & Surveillance Unit, contacted the Alzheimers Society to see if they would set up a formal CJD Support Network. It took three years and during this time, because of BSE, CJD went from being little known to become a high-profile disease.

Sadly, Graham decided in 1996 that he should stand down from being a committee member of the Network, to concentrate on his family. But he did not forget us. He has telephoned me at least once a year for a long call.

We have come to know Graham well, particularly for his knowledge of the field of CJD



The Blades family and (right) Janet Blades

and his devotion to his family. His life was caring for Janet and their children.

Sadly, on 15 February 2017, Janet passed away. Graham awaits the findings of a post-mortem to learn what was wrong with Janet. Graham cared for Janet, who had a 'working diagnosis' of CJD, for 29 years.

# Understanding prion structure

Dr Jonathan Wadsworth  
Programme Leader  
MRC Prion Unit  
University College London



Prions, the infectious agents causing BSE in cows and CJD in humans, are unique in medical research.

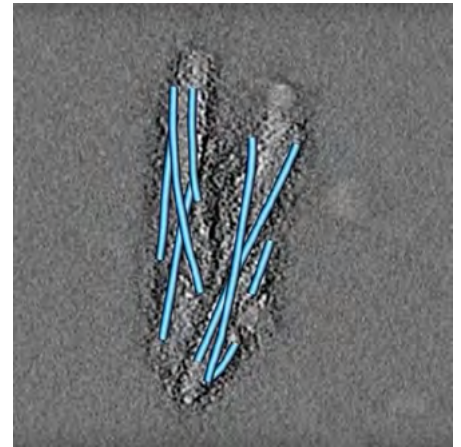
Unlike all other infectious agents (bacteria and viruses) the infectious particle does not contain genetic information (genes) but instead consists of clumps of misshapen, rogue forms of one of the body's own proteins called the prion protein. Once formed in the body, rogue prion proteins act as seeds to convert normal prion protein into a likeness of themselves setting off a chain reaction leading to progressive accumulation of the rogue protein in the brain. This ultimately causes the death of nerves resulting in the neurological symptoms of prion disease.

Although prions do not carry genetic material they come in several different forms, called prion strains that cause different forms of the disease. Our long-term research aim has been to understand the fundamental biology of what makes prion strains different from one another and why some are able to cross from animals to humans to cause disease. Our work focuses on isolating infectious prion particles from diseased tissue and using sophisticated equipment to study their chemical makeup and three-

dimensional structure. For some of our studies we use model prion strains from mice whose infectivity can be detected in isolated cells allowing us to make much faster progress than has been previously possible. Through this work we hope to provide a detailed description of the misshapen prion protein structures that are associated with each prion strain and pinpoint exactly what differences are responsible for a particular form of the disease.

Understanding what is special about the structure of prions is increasingly important as it is thought that similar processes, with the spread of growing misshapen protein seeds, are also involved in the commoner neurodegenerative conditions such as Alzheimer's and Parkinson's diseases. Over the years our research has been actively supported by the CJD Support Network (CJDSN) who kindly provided us with a PhD student scholarship endowment and we have previously written research updates for the CJDSN newsletter and given research talks at family support days. Our research would not be possible without the support of patients and their families and we are extremely grateful to them for their consent to use human tissues in our research.

Recently, after considerable effort to develop and optimise new methods for prion isolation, we were able to obtain the first three-dimensional images of isolated infectious prion particles. Our findings were reported last year in the journal *Open Biology* which is published by The Royal Society. We showed



Electron microscopy was used to help construct 3D images of prion proteins

that during infection, rogue prion proteins in the brain assemble into infectious rod-like structures that are formed from twisted pairs of short double helical prion protein fibres. This novel structure is common to multiple prion strains that we have examined and is distinct from non-infectious prion protein structures that can be artificially generated in the laboratory. The architecture of natural infectious prions that we have described now provides a new structural basis for understanding their distinctive properties. Presently, using new funding from the Medical Research Council, we are working hard to understand prion structure in much greater detail. This information might provide important new clues to ways of stopping the disease process and might enable the rational design of new effective treatments for patients.

*For readers who are interested, our Open Biology paper can be accessed from this link: <http://rsob.royalsocietypublishing.org/content/6/15/160035>*

# Reducing the risk of iatrogenic transmission of CJD by improving the cleaning of neurosurgical instruments

University of Glasgow: AJ Smith, T Tomkinson & DF Lappin

## The emergence of vCJD in the UK has raised concerns over the possible risks of transmission of iatrogenic prion disease due to its resistance to inactivation processes such as steam sterilization.

Of particular concern is the high levels of infectivity found in tissues classed as high risk for CJD (central nervous system and posterior orbit of eye) and the potential for residual infectious material to remain on instruments following cleaning and sterilization. There are currently no reported cases of vCJD due to cross-contamination of surgical instruments. However, risk assessments stress the importance of ensuring a high quality of current cleaning and sterilization processes. While the absolute risk of CJD transmission via contaminated surgical instruments is low, the potential risk has led to the development of a series of measures to limit transmission.

An unintended consequence of the move to larger Sterile Service Departments (SSDs) which are

serving several theatre complexes in different hospitals is that there is an increase in the time prior to the cleaning and sterilization of surgical instruments. Several workers have demonstrated that as the drying time (>15 minutes) increases, instrument residues from theatre become more difficult to remove, increasing risks of iatrogenic diseases transmission. To overcome this problem, workers and Department of Health policy statements have suggested using either spray/foam agents or polythene bags to keep the instruments moist from point of use until cleaned.

Many of the studies that have investigated methods for retaining moisture around surgical instruments prior to decontamination have been undertaken on stainless steel tokens contaminated with

artificial test soils and laboratory washing protocols.

There is little published work that has investigated the application of instrument pre-treatment protocols under operating theatre and SSD conditions. Anecdotal reports have suggested that some pre-treatment chemicals may impair the function of the instrument washers or protect the soiling on the instruments from detergent action in the wash process.

Our group has obtained funding from the Scottish Infection Research Network (SIRN) to investigate a number of different pre-treatment methods to improve the cleanability of neurosurgical instruments. A number of different formulations will be screened in the laboratory and the two best performing agents will be trialed in the field with close collaboration with neurosurgeons, theatre staff, engineers and staff at the Cowllairs SSD. Improvements in cleaning will be monitored by measuring residual protein using biochemical assays contained in the British, European and International standard alongside a novel technique developed by Professor David Perrett and Dr Nanda Nayuni that visualizes residual protein on surgical instruments (see figure 1).

The success of this project is due to a collaborative approach between the following groups of organisations and people: University of Glasgow: AJ Smith, T Tomkinson & DF Lappin · NHS GG&C, Neurosurgery Dept: P Pamela & N Suttner · Cowllairs SSD: I McIvor, A Stewart, S McWilliam & C Ladjadj · Health Facilities Scotland: S Holmes, R Allan, D Ingle, D Hill, P Howard, L Palmer, S Murphy & N McLean · Queen Mary University of London: D Perrett & NK Nayuni

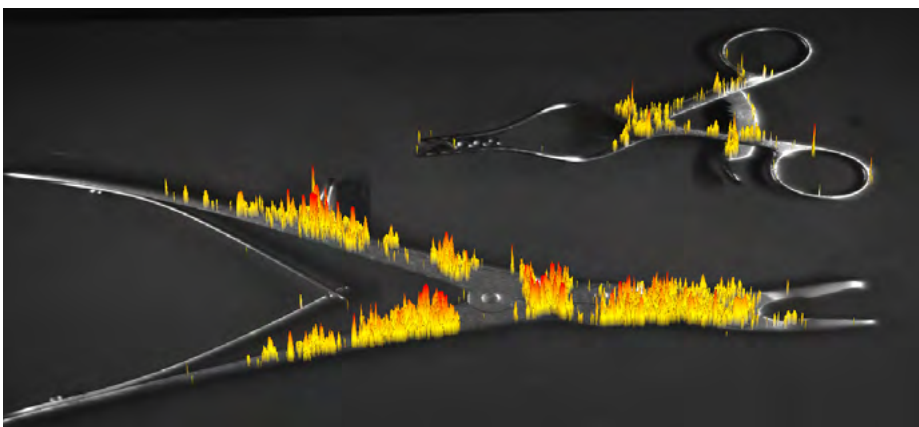


Figure 1: A ProReveal system 3D-fluorescence image of surgical instruments prior to the cleaning cycle. The residual protein is shown (yellow to red, which represents the relative protein concentration)

# The role of the CJD Research and Resource Centre at the National Institute for Biological Standards and Control (NIBSC)



**Dr Philip Minor, Head of Virology Division, National Institute for Biological Standards and Control, gives an overview of the role NIBSC has in assessing possible diagnostic tests for CJD and in collecting scarce patient samples to help in the development of tests.**

## The need for a test for CJD

There is still a need for a reliable test to identify individuals incubating CJD and vCJD in particular. Those who have been informed that they are at higher risk of infection because of medical or other treatments may wish to know whether they are really infected or not; from a public health point of view it would be helpful to identify people who are potentially infectious for others, so that spread for example through blood transfusion could be prevented. Complicated precautions and models have been developed to minimise possible onward spread and to predict future incidence of disease. All are based on worst case assumptions including estimates of the incidence of currently silent infection which have been hard to come by and are not that certain.

## The problems in developing a test

Development of a test for any infection is always fraught; a test that incorrectly misses an infected sample or incorrectly identifies a normal sample as infected has major bad effects for the patient and the public health system. Tests for CJD are even more difficult than most because the infected state is almost entirely without symptoms or any marker of infection before symptoms develop. Virus infections are associated with virus specific nucleic acids or proteins or antibodies made by the patient against the virus and assays for infection can be based on these

associations which do not exist for CJD. In addition the number of cases is thankfully smaller than for most other infections; it is not hard to get a thousand specimens for developing a test for Hepatitis B for instance which would be unthinkable for vCJD. Moreover vCJD is a stealthy and frightening disease, so in the early days at least the desire for a test was very great, which created the possibility of poor tests being developed and used. There needed to be some kind of objective scientific evaluation and judgement of tests in development, to see if they were likely to give reasonable results when tested with the scarce real patient samples.

## NIBSC

The Department of Health therefore funded NIBSC to establish a collection of samples relevant to test development and devise a route by which promising tests could get access to the few real samples from patients that were available. The centre provides a clear if torturous route for developers to do this and the Oversight Committee considers proposals for studies and guides its activities.

## The Oversight Committee

The Oversight Committee was set up to include all groups that might have a technical interest or ability in CJD test development. It is intended to access the best possible relevant scientific advice and includes CJD scientists and medical experts from the MRC Prion Unit and Edinburgh

Research and Surveillance Centre, as well as scientists from the agricultural sector with an interest in BSE or scrapie and possible diagnostics being developed there. Public Health England (PHE) and the blood services are included.

Tests for CJD are even more difficult than most because the infected state is almost entirely without any marker of infection before symptoms develop

NIBSC organises the meetings and brings proposals and results to the committee for discussion. Developers are identified through scientific contacts and meetings and are usually contacted by NIBSC scientists, but things can be brought into the system through other committees such as the Prion Working Group (PWG) of the blood transfusion service or the TSE working group of the Advisory Committee on Dangerous Pathogens (ACDP). The idea is to be as inclusive as possible. Most of the meetings are face to face unless an urgent response is needed and a meeting proves difficult to organise.

Developers who wish to access samples through the committee follow an established route, with the results being discussed at each stage by the committee members, to see if it is good enough to continue to the next step. It is up to the developer to decide whether they wish to continue; they may fail at a step, but if they wish to modify the assay and have another go that is welcomed.

**Blood test**  
Blood is the easiest sample to get for testing and the amount of infectivity in blood is known to be low. The initial evaluation involves measuring



## The Cure CJD Campaign

# Potential new treatment to be tested

the sensitivity of the test by trying it out on samples that are known to be infectious, such as dilutions of infected brain. Blood samples from healthy donors are then tested to establish whether the test incorrectly scores samples positive.

This has been followed by the use of samples from animal models which are easier to obtain; assuming the test will work on animal samples, this can show that detecting signals is possible. It is also possible to look at animal samples in the preclinical stage, which have been shown to be infectious, for example by transfusion to recipient animals. If a test cannot detect such samples it is obviously not much good in practice.

The experiments needed to collect these kinds of materials take a very long time to complete and are very complicated to organise and deliver, but the Centre has a very extensive archive of materials, produced by a beautiful study at the Roslin Institute in Edinburgh, which is proving invaluable in assessing test performance on preclinical samples, which are the ones you most want to test. The preclinical samples seem to have less of the marker of infection than those from clinical affected animals and the same is probably true in humans. This presents another hurdle because samples from preclinical human cases are almost non-existent although there are a few from blood donors who went on to develop the disease.

The net result of this has been slow progress and a number of honourable failures, but as of now there seem to be two blood tests, one in France, the other in America which look very promising. One of them is very near the stage of CE marking, which is part of the process by which a diagnostic test is approved for use in Europe.

**As many readers know from personal experience, there is currently no cure for Creutzfeldt-Jakob (CJD). However, scientists and doctors believe that they are getting closer to finding a treatment.**

Prion diseases are rare and particularly challenging for the development of treatments. In other infections, the immune system recognises foreign proteins and other parts of germs as being alien to the body and this leads to the body producing specific antibodies tailored to fight that infection. However, since prions are formed from one of the body's own proteins they are not recognised in the same way by the immune system and lifesaving antibodies are not produced. This is one of the reasons why prions are so lethal.

Researchers at the MRC Prion Unit and other researchers around the world, have conducted long-term research to investigate potential antibody

treatments for prion disease and to see if such treatments might work and what side effects or other safety issues might be anticipated. The MRC Prion Unit has developed a potential antibody therapy which they are preparing to test clinically for the first time in a small number of UK patients with sporadic CJD. The Cure CJD Campaign is a group of individuals personally affected by the disease who are raising funds to support this.

For more information, please see the Cure CJD Campaign website [www.curecjd.org](http://www.curecjd.org) where you can see our video explaining how the potential treatment might work. To donate to the Campaign, please visit our Just Giving page [www.justgiving.com/cure-cjd](http://www.justgiving.com/cure-cjd)

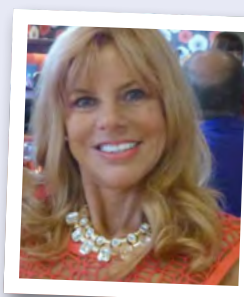
## Calendar girls for CJD

by Lesley-Ann Allen

Beryl, my amazing mum, lost her five month's battle with sporadic CJD, passing away in October 2013. I am of a certain age (55) as are all my friends and I thought long and hard about what to do to raise money for CJD in a different way. So on the 18 June 2017, fifteen menopausal ladies are creating a 'calendar girls' calendar, with



our own twist on it! Each month will then hopefully be sponsored by businesses in the area. The calendar will be ready for sale around September.



## My brother Mark

by Karen Goodall



After several months of GP appointments, various tests and hospital visits, my brother Mark, was finally diagnosed with vCJD in August 2015 at the age of 36.

We first noticed that there was something wrong around a year prior to this. Mark had become quite withdrawn and had problems with his balance, which meant he became confined to a wheelchair, just the kind of thing you would want for a six foot two 16 stone scaffolder!

I found that his short-term memory was poor but bygone events such as nights out and meeting old acquaintances were recapped as if they occurred the previous day. As Mark's condition declined we were unable to have conversations with him and on Tuesday 23rd February 2016, he passed away, surrounded by his family.

During the illness, it was a blessing that Mark was not aware of his condition and the ultimate outcome.

## My granddad

by Jenny Sandall

The start of 2015 shocked my family and me, as my 69-year-old grandfather Michael Glenn Rumsey (Mick) was taken into hospital.

At first, the hospital was sure that he had suffered from a Stroke. Scientists rushed from Edinburgh to the Norfolk and Norwich NHS Hospital to do tests, which resulted into an accurate diagnosis. It was three months before they gave him his full diagnosis of

CJD. 'One in a million' the doctors had said.

Everyone that has known my grandfather would have told you about his bravery, strength and incredible love for his family and friends. For him to deteriorate the way he did and as quickly as he did, was unnatural and heartbreaking to see. Worst of all, there wasn't a single thing we could do to stop it.

Michael Glenn Rumsey (Mick) sadly passed away on March 26 2015 in a care home close to home. He was surrounded by loved ones and was peaceful.



Mick Rumsby is on the right

## Living with Genetic CJD

Anita Judd

My family are affected by Inherited Prion Disease (genetic CJD). We discovered this devastating condition in my family in 2000.

Living with a rare hereditary condition like Genetic CJD in your family is devastating and can be very overwhelming. It's always there, always in the background, affecting the things you do and the decisions you make in life.

Discovering genetic CJD in my family has been life changing for me and other members of my family.

I sometimes think of the time when we were unaware of it. However, I think myself and other members of my family have changed our lives for the better because of it, with the realization of how precious life is.

## Amanda Harding

by Catherine Campbell



Amanda with her grandson Bertie

Last November, a well-known Gloucestershire woman, Amanda Harding, sadly died of the sporadic form of CJD.

She began to have problems with her balance last spring. At first it was thought to be vertigo. She was finally diagnosed CJD and the end was quick and peaceful. It was a blessing that throughout her illness Mandy suffered no pain and was unaware of how terminal her illness was.

Mandy left behind her husband, Michael, her two children, Oliver and Laura, and her grandson, Bertie. Mandy was passionate about horses and rode the whole of her life. Her family hosted a meet of the Berkeley hounds in February, which was very well attended. People dug deep into their pockets and all the money raised (£2,383) went to the CJD Support Network to fund further much needed research.

Michael would like to thank everybody who donated so generously in Mandy's memory. She is fondly remembered by all and greatly missed.

## Margaret Ann Lee

by Terence Lee

My dear wife Margaret passed away due to sporadic CJD in 2014. I would like to share my experience of this time.

We had been married for 43 years and were very close. We worked together on a family basis in our own business for 30 years. We retired in 2013 and were looking forward to some quality leisure time together.

In early June 2014, when out shopping, Margaret could not find items in the supermarket she regularly shopped in. She became withdrawn. We consulted the local GP, who gave her a dementia test and took blood samples. Both were negative and it was suggested that Margaret had depression. I was adamant that it was not, knowing Margaret better than anyone.

During the next three visits, various medications were prescribed, each making her feel wretched. On the 12 June, a fourth doctor could see that swift action was needed and arranged a CT scan. Within ten days Margaret had deteriorated to an extent that she did not know where to find items in the kitchen and could not remember how to carry out tasks, or which door led to which room. She became very frightened and emotional.

On 16 June the results of the CAT scan were negative, but the GP could see that a marked deterioration had taken place. Margaret was admitted to the Worcester Royal Hospital Medical Assessment Unit for further tests.

The following Wednesday a lumbar puncture was taken – all the time Margaret was deteriorating; hallucinating and falling out of bed. An MRI scan was carried out and



Margaret Ann Lee  
16 July 1947 – 8 July 2014

on the Tuesday, a neurologist saw Margaret. His conclusion was again depression. On the Wednesday, a further lumbar puncture was taken. She was very distressed and frightened. A doctor came and stood at the end of the bed and said 'you may have CJD, you know, that cow disease!'. Although Margaret was not fully aware, she did recognise the implications and spoke to me about the end of her life. The situation was very distressing but I tried to remain positive. I insisted she was discharged and on Friday of that week she arrived home.

Deterioration was rapid and the hallucinations were becoming violent. Margaret imagined that the IRA were there to blow us up. I had to pin her down on the bed to keep her safe. I finally realised that I could not cope. I had to break a promise that I would look after her at home and found a place in a local nursing home.

On Wednesday 2 July, Dr Irwin and Blaire Smith Bathgate flew down to Worcestershire and spent time with us. Dr Irwin was very kind and gentle with Margaret while Blaire spoke to the nursing staff about what to expect.

On 6 July Margaret slipped into unconsciousness and finally passed away on 8 July at 10.50pm.

# The 65+ Study

Dr Anna Molesworth and Professor Richard Knight  
National CJD Research and Surveillance Unit

## Sporadic CJD and age

Sporadic CJD (sCJD) is the commonest form of human prion disease. It occurs sporadically (hence the name) in all countries where it has been looked for and is, essentially, of unknown cause.

Risk factors are things that increase one's chances of getting a disease, while not being the only cause or necessarily leading to disease. Extensive studies of sCJD have not identified any major consistent risk factors aside from age and having a particular genetic form of the prion protein (the 129-MM genotype).

Some other genetic factors have been identified as playing a minor role and some studies have suggested that surgical procedures might be a risk factor in some cases. However, the most widely held view on sCJD is that it occurs spontaneously due to a chance protein abnormality.

If this view is correct, then one might expect age to be a risk factor. This is because, firstly, the longer one lives, the greater the chance of some random protein error and, secondly, ageing might be associated with a deterioration in any biological mechanisms that detect and deal with these protein errors.

However, there is one well-established observation concerning age and sCJD: the disease is very rare under 40 years of age, becomes more common with increasing age

up to around the age of 65 and then it declines somewhat in frequency. This fall in incidence in the older population is not definitely explained, but there are two general views:

- 1) It represents under-diagnosis in the over 65s and
- 2) sCJD is genuinely less common in this age group. In the older population, the incidence of other dementing illnesses, which might resemble CJD, is high.

In addition, the absolute diagnosis of CJD depends on neuropathological examination of the brain but this requires a post mortem examination, rates of which are very low in dementing illnesses in the elderly. On the other hand, if sCJD incidence genuinely falls in the elderly, this might tell us something important about its cause.

## Variant CJD and age

Variant CJD (related to BSE) has affected a much younger age group than sCJD. There are explanations of why this might happen, but it has been suggested that cases might also be missed in older people, perhaps mistaken for other more common dementing illnesses.

## The 65+ Study

In order to address these uncertainties, the UK Department of Health has funded a study to try to ascertain if there are missed cases of CJD in the older population. The

study is based at the National CJD Research & Surveillance Unit in Edinburgh and headed by Dr Anna Molesworth. The long-running UK CJD surveillance system relies on notification of suspected cases by clinicians and, in its course, it has picked up many cases of CJD in the older population. However, to ascertain if cases have been missed, one needs to establish an intensive focus on older people with dementing illnesses that may not be suspected as having CJD. In order to attempt this, the researchers need to liaise closely with routine memory/dementia services, covered by Neurology and Old Age Psychiatry services, as well as Medicine for the Elderly. As there are significant numbers of patients attending such services, it was decided, as a first step, to undertake a feasibility study based on a limited geographical area (the Lothian area in and around Edinburgh).

The study began in 2015 and has been collecting detailed information since 2016. There are no specific results to report at this stage, however this represents a potentially important intensive surveillance addition to the well-established UK CJD surveillance system.

*More information about the 65+ Study can be found online at <http://www.cjd.ed.ac.uk/projects/all-projects/65-dementia-study-enhanced-surveillance-creutzfeldt-jakob-disease-older>*

# Donations in memory

Heartfelt thanks to the families and friends of those below for donations received between March 2016 and April 2017 in their memory

Julian Bailey

Margaret and Alan Bedford

Anna Bellerby

Barbara Betty Bennett

Janet Blades

Brenda Boseley

Seamus Boyce

Rita Ann Brown

Denise Clewes

Peter John Closey

Chris Collins

Pat Conlon

John Cutting

Danny Doherty

Carole Gibbins

Amanda Elizabeth Harding

Maxine Hayes

Wynford Jones

Lyndon Lloyd

Danny Martell

Darren Matthews

Peter Milton

Maureen Mitchell

Margaret Mary O'Sullivan

David Phillips

Mark Pope

Sarah Ridgwell

John Saunders

Mr Smitherd

Mrs M Thompson

Trevor Paul Wallis

Alan Walsh

Patrick Wellings

Barbara Wright

Linda Young

## UK CJD figures

Recent numbers of deaths of definite and probable cases in the UK.  
Figures from the National CJD Research and Surveillance Unit in Edinburgh

Year	Sporadic	Iatrogenic	Genetic	vCJD	Total
2012	93	5	11	0	109
2013	106	2	8	1	117
2014	99	3	11	0	113
2015	104	0	4	0	108
2016	110	1	4	1	116
2017*	26	0	1	0	27

\* As at 3 April 2017

Source: [www.cjd.ed.ac.uk](http://www.cjd.ed.ac.uk)

**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. If you would like to become a member of the CJD Support Network and receive free regular copies of our newsletters and any other information we produce, please complete the form below and post to the CJD Support Network, PO Box 346, Market Drayton, Shropshire TF9 4WN. Membership is free, but we welcome donations.

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