CJD SUPPORT NETWORK

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Newsletter

Issue 28
July 2019

CREUTZFELDT-JAKOB DISEASE SUPPORT NETWORK NEWSLETTER

Pioneering treatment for CJD

Professor Simon Mead
MRC Prion Unit

A small number of patients of University College London Hospitals NHS Foundation Trust (UCLH) have been given a pioneering treatment for Creutzfeldt-Jakob disease

Researchers at the Medical Research Council (MRC) Prion Unit at University College London (UCL) have developed an antibody, called PRN100, for treating CJD. Laboratory testing of the antibody has been encouraging but until October 2018 it had not actually been used on patients.

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 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, the agent that causes CJD and other prion diseases, 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.

An artifical antibody, PRN100, has been developed to prevent rogue prions binding to healthy prions and causing devastation in the brain

IMAGE TAKEN FROM VIDEO BY CHRIS BEATTY FOR MRC PRION UNIT
SEE WWW.CURECJD.ORG/PRION-DISEASES

PRN100 is an antibody specifically designed to bind tightly to the normal prion 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 been found to have potent activity in laboratory test models of prion disease. Laboratory tests provided a 'proof of principle' that PRN100 works by preventing the chain reaction and the formation of new prions.

In a world-first, the antibody was given to a patient of UCLH in October 2018 after a judge in the Court of Protection confirmed that it was lawful and in the patient's best interests to receive the unlicensed treatment.

UCLH has subsequently given the drug to a small number of additional patients.

UCLH's chief executive Professor Marcel Levi said: 'Creutzfeldt-Jakob disease (CJD) is a rare and cruel disease which rapidly destroys the brain, affecting memory, thinking, speech, balance, movement and behaviour. There is currently no cure or treatment for CJD. At present, caring for patients with CJD involves trying to use medicines to alleviate symptoms only but sadly, the disease always results in the rapid death of the patient.'

Professor John Collinge, Director of the MRC Prion Unit at UCL, who led the development of the PRN100 treatment, said: 'The treatment is an artificially manufactured antibody which has been created in the laboratory. The antibody has been designed to bind tightly to normal proteins in the brain. The aim is to prevent

abnormal prions from being able to attach themselves to healthy proteins, meaning that they cannot grow and cause devastation throughout the brain.

'The patients who have received the antibody so far have been at different stages of their disease when they began treatment. It is too early to determine if, or to what extent, the drug has had an impact on their condition.'

The treatment is given by a drip into a vein in the arm with monitoring around the clock from experts.

UCLH is prepared for a range of possible outcomes including the treatment causing harm or having no measurable effect to the treatment slowing or halting the progression of the disease. The treatment was not expected to reverse any brain damage that has already occurred.

In order to provide this treatment, UCLH created an oversight group, independent of the MRC Prion Unit and treating clinicians. The group comprises world-leading experts from a range of disciplines and it has met regularly with lawyers and patient advocates. The group considered the numerous and complex clinical, safety, legal and ethical issues arising from the potential use of this unlicensed treatment for CJD.

If you would like to enquire about PRN100 treatment, the National Prion Clinic can be contacted at uclh.prion.help@nhs.net

For further written information please visit a frequently asked questions section at the UCLH website: www.uclh.nhs.uk/OurServices/ServiceA-Z/Neuro/NPC/Pages/PriondiseasesandCJD.aspx

You can watch a video about how the antibody might work here: www.curecjd.org/prion-diseases

CJD Support Network Family Support Meeting 2019

15–16 November 2019
Burlington Hotel, New Street, Birmingham B2 4JQ

The CJD Support Network management committee would like to invite you to our annual family support meeting in Birmingham.

Our 2018 family support meeting was our best yet. We followed our members' request to provide more time for families to meet and share their experiences by hosting a welcome reception and dinner on the Friday. This proved very successful and we had some lovely feedback.

This year, the reception and dinner will be on Friday 15 November at 7pm. Whilst 2018 was very successful, it was also expensive for the Network, so this year we are asking for a £10 per person contribution to the dinner. There will be no charge for the formal meeting and lunch on the Saturday. The £10 contribution for the Friday is to help with the costs, and hopefully will also stop people from registering but then not attending on the Friday evening. Last year we had eight 'no shows' who we still had to pay for. If you wish to come to the dinner, registering is essential.

If you want to stay overnight at the Burlington Hotel on the Friday night, a special discount has been arranged by us. If you want to stay at the Burlington Hotel please book your accommodation quoting the discount code directly with the hotel.

To get this hotel discount code and to attend either the Friday dinner or the Saturday meeting you must contact and register with Gillian Turner on 0800 0853527.

Programme

Friday 15 November

19:00	Pre-dinner drinks reception
19:45	Dinner

Saturday 16 November

09.30–10.00	Registration/coffee/tea
10.00–10.05	Welcome: Prof Richard Knight
10.05–10.10	Brief Introductions of Committee Members: ALL
10.10–10.30	Ice Breaker/Mixing: Prof Simon Mead
10.30–11.00	Introduction to Prion Disease/CJD: Dr Kiran Jayaprakash
11.00–11.05	Q & A
11.05–11.30	Bereavement: Bethan Marsh
11.30–11.35	Q & A
11.35–11.50	Morning Break
11.50–12.20	Research Presentations: Dr Akin Nihat, Dr Tzehow Mok
12.20–13.00	Q & A
13.00–13.45	Lunch
13.45–14.00	AGM
14.00–14.25	Where are we with Treatment? Prof Simon Mead
14.25–14.30	Q&A/Discussion
14.30–15.30	Round Table / Informal Discussions
15.30–1600	Close: Prof Richard Knight

Summaries of talks delivered by key speakers at our November 2018 Family Support Meeting

First of all, Prof Knight touched on the basic biology of the human body ie. the cell, proteins, amino acids, chromosomes, genes, neurons and synapses.

Introduction to prion disease

Prof Richard Knight

Different organs in the human body have different cells that reflect their functions. A cell has a nucleus and it is the basic structure and functional unit of an organism and everything that we do depends on how well the neurons function.

The brain is made up of a variety of cells. Within the brain, functions are localized to particular areas of the brain like vision, coordination, memory, language and motor control.

Neurons are nerve cells and are electrically active communicating with each other. The synapse is the conduit between two neurons which transmit information by electrical and chemical signals. If the synapses malfunction the network breaks down and problems will develop.

Proteins form the structure, function and regulation of the body's tissues and organs. Amino acids are the building blocks of proteins and their functions depend on its final chain.

Proteins are made in the cell nucleus. The cell nucleus contains 46 chromosomes where 23 pairs come from each parent. The chromosome contains a gene which is a string of code. The code is translated in a chain of amino acids and mistakes can occur in a string of code ie. addition, deletion or altered.

A change in gene code results in a change in the amino acids. There are two types of gene code:

- Pathogenic mutation causes disease.
- Polymorphism is where a minor change has occurred which does not directly cause disease. However, it may affect one's susceptibility to the disease.

What is CJD?

It is a prion disease and it is transmissible.

Normal prion protein (PRPc) is a protein that our body produces.

The normal prion protein undergoes a change in conformation into abnormal protein (PrPsc). PrPsc protein is the final arbiter for the diagnosis evident to CJD patients.

People develop symptoms and become ill because neurons malfunction and die.

Neurological symptoms and disability are progressive. Infection requires an infective agent and the PrPsc prion is the infective agent.

Types of the disease

Idiopathic sCJD
The most common form of CJD and very rare among the young. It is notable among individuals over 50 years of age and declines after 65 years of age. It is rapid and progressive.

Acquired CJD
Kuru, iatrogenic CJD, vCJD and secondary transmission.

Genetic prion disease
Is autosomal dominant inherited prion disease. Siblings have a 50/50 chance of contracting the disease. This prion disease includes: Genetic CJD, Gerstmann-Straussler-Scheinker (GSS) and Fatal Familial Insomnia (FFI).

Diagnosis

Requires brain biopsy in life and brain autopsy on death.

Clinical diagnosis must have a suggestive clinical picture and the exclusion of other possible diagnosis/tests that will help scientific diagnosis.

Tests to support scientific diagnosis

Non-specific tests includes EEG, MRI and CSF for 14-3-3 test. The results are not unique to prion disease and therefore need careful assessment.

A specific test is a test related to specific process ie. a test detecting the abnormal gene. The biggest change is the CSF RT Quick test which detects the abnormal protein if one has the disease. Tonsil biopsy is useful for vCJD.

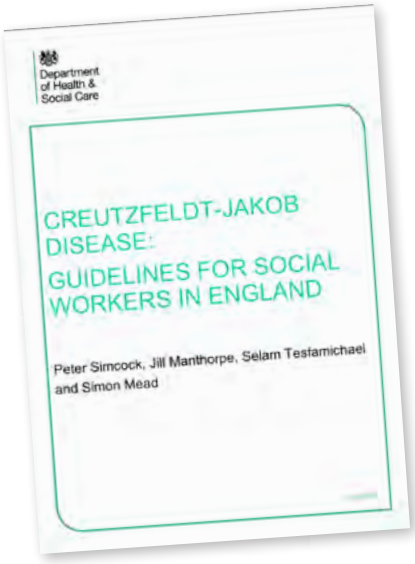
Nasal brushing, skin biopsy and urine test are not validated and therefore not used as a normal routine for diagnosis.

Some tests are relevant only to specific types of prion disease.

Points to consider when making a clinical diagnosis

- Onset of prion illness is often non-specific
- Passage of time maybe a diagnostic tool
- Exclusion of other possible diseases takes time
- Other diagnosis maybe treatable
- Atypical prion disease is difficult to diagnose
- Emerging specific tests are changing diagnosis

Peter Simcock gave a brief background of the Social Work Guidelines. The first set of Guidelines (1998) were authored by Derek Biggs: 'Guideline on CJD for Health workers' (DH 2000) and 'Updated Social Services Guidelines' (Biggs 2003). The Guideline have been updated since and the current version can be accessed online (see below).



Updated guidelines for social workers

Peter Simcock

Introduction

CJD is a rare disease and it is outside of the most experienced of social workers. Timely and speedy responses to the clients' needs are of the essence and urgency to provide that need is required. Speedy responses are needed and services should be personalized according to the need of the person.

NHS Continuing Health Care

The NHS provides the primary care to people who need it. Local authority cannot provide what the NHS can provide but the local authority representative can access the threshold. It is essential that people are aware of what they are entitled to.

Reasons for updating the guidelines

Well-being principle (Care Act 2014) – it is the statutory duty of the local authority to promote individual wellbeing which includes family relation, social care and recognizing the stimuli to help individuals do something for themselves. It is about maintaining the dignity in the relationship between the local authority and the individual.

National Eligibility – needs must be related to the physical and mental ability in managing and maintaining a habitable home. Eligibility does not depend on one's diagnosis. Well-being does impact on it and an assessment will be required.

Carers' Right – carers are entitled to an assessment of their needs by the local authority. The local authority has a duty to meet their needs. The carers' right enables people to relocate and carry on without encountering any difficulties in their entitlements so that there won't be any gap in providing the service.

Mental Capacity Act 2005 – it is the statutory framework for the assessment of needs in the best interest of the individual. It clarifies who can make the decision and necessary steps taken in the event of loss of mental capacity of the individual. The Act enables the individual to plan ahead.

Fast Tract Pathway Tools – refers to the pathway for clients at end of life.

The latest Guidelines for Social Workers can be viewed and downloaded from the Fact Sheets box at www.cjdsupport.net. The Guidelines are the last factsheet on that page.

The Treasurer presented his full financial report and accounts at the AGM. This is a brief summary of key points made by Andy:

Financial Report

By Andy Tomaso

The Network's income during the year end 2018 is down compared to 2017. However, we still managed to generate a surplus to ensure our reserve balance continue to grow. This reserve will enable the Network to keep operating for three consecutive years, as well as fund the two research projects described elsewhere in this newsletter

As it stands the Network is in good financial footing, however, as we receive no statutory funding, we rely heavily on the fundraising events and donations from our generous members and friends of the Network.

Thank you to all members and friends of the Network who have fundraised and donated during the year to keep the Network going and allow us to continue supporting families.

The Family Support Meeting will be held in Birmingham again this year, 15–16 November.

All are welcome but registration with the Network is essential.

See page 2 for details.

Retirement of Professor Bob Will

By Chair and members of the CJDSN Management Committee

Professor Bob Will, known to many families in the UK and around the world, retired on 31 March 2019.

On the medical and research side, in 1990, he set up the National CJD Surveillance Unit (now the National CJD Research and Surveillance Unit), based in Edinburgh and was its director for many years. Along with his colleagues, he identified the occurrence of variant CJD and made significant contributions to proving its cause in dietary contamination with BSE.

Apart from this specific discovery, he made major contributions to understanding the epidemiology, clinical features and diagnosis of prion diseases in general. He established and led an international research and surveillance collaborative network, enabling the collection and analysis of large amounts of data which would otherwise not have been possible with a rare disease.

Although these research contributions have been of great importance, Bob Will was, at heart, a clinician; the care of those with CJD and their families remained of paramount importance to him. For many years, he oversaw the UK Care Package which has helped many families. He was pivotal in the establishment of the UK CJD Support Network and contributed much to the Network over many years. He also contributed much to other support organisations, especially the USA CJD Foundation and the Australian CJD Support Group Network.

Those families who have attended meetings at which he spoke, will know and appreciate that he was able to present research in terms that could be readily understood by non-experts. He was a modest individual to the point that he would probably prefer this notice to be limited to a single sentence, simply stating that he had retired, however, the CJD Support Network feel it important to note and thank him for his considerable contributions. Many friends, colleagues and family members will miss him and all would want to wish him a happy retirement.

Deaths from definite or probable CJD

Source:
National CJD Surveillance Unit
www.cjd.ed.ac.uk

Year	*Sporadic*	*Iatrogenic*	*Genetic*	*vCJD*	*Total*
1990	28	5	0	-	**33**
1991	31	1	4	-	**36**
1992	45	2	6	-	**53**
1993	36	4	7	-	**47**
1994	53	1	9	-	**63**
1995	35	4	5	3	**47**
1996	40	4	6	10	**60**
1997	59	6	6	10	**81**
1998	64	3	5	18	**90**
1999	62	6	2	15	**85**
2000	48	1	3	28	**80**
2001	58	4	6	20	**88**
2002	73	0	5	17	**95**
2003	79	5	6	18	**108**
2004	50	2	6	9	**67**
2005	67	4	13	5	**89**
2006	68	1	9	5	**83**
2007	63	2	11	5	**81**
2008	84	5	6	2	**97**
2009	78	2	8	3	**91**
2010	85	3	6	3	**97**
2011	91	4	14	5	**114**
2012	94	5	11	0	**110**
2013	108	2	10	1	**121**
2014	99	3	13	0	**115**
2015	105	0	4	0	**109**
2016	117	1	6	1	**125**
2017	121	0	12	0	**133**
2018	135	2	11	0	**148**
2019*	56	0	1	0	**57**
Total	**1962**	**80**	**194**	**178**	**2414**

* As at 1 July 2019

Improving palliative care for people with CJD and their families

Dr Liz Sampson, Clinical Reader and EMBED-Care Principal Investigator

There are many misconceptions about palliative care. It is not about withdrawing or limiting care, but about managing symptoms such as pain and other causes of distress. Palliative care focuses on quality of life for people with life-limiting illness and their family. It is not just accessed through hospices but can be delivered in a person's own home, with support from their GP and other community services, or in a hospital. Dame Cicely Saunders the founder of the modern palliative care movement said, 'You matter because you are you and you matter to the end of your life. We will do all we can not only to help you die peacefully, but also to live until you die'.

This is a neglected area for people with neurodegenerative diseases such as CJD. Some people receive good care at the end of their lives, but others do not. CJD can progress rapidly and symptoms can change quickly. There may not be time for referral to palliative care services and staff may struggle as they have little experience of caring for people with CJD.

A person with advanced CJD may experience treatable symptoms but may be unable to communicate their pain or other problems. Families may have to adapt rapidly to the diagnosis. Loss and grief can occur before and after the person with CJD has died. The genetic nature of some forms of CJD brings additional concerns.

The Marie Curie Palliative Care Research Department at UCL works with people who may have difficulty accessing palliative care. Our Centre for Dementia Palliative Care Research is a growing team with expertise in psychology, social sciences, palliative care, geriatrics, old age psychiatry and dementia care. We have been funded by the UK Economic and Social Research Council and the National Institute for Health Research, in partnership with the Cicely Saunders Institute at Kings College, London, to run the Empowering Better End of Life Care in Dementia (EMBED-Care) research programme.

Over the next five years we will drive forward evidence, policy and palliative care services for people with dementia who may benefit from palliative care. Working with Professor Simon Mead and the National Prion Clinic we will do the first studies on palliative care for people with CJD. We will collect information on problems including pain, agitation, difficulties swallowing and family carer grief and distress. We will use a new tool – the Integrated Palliative care Outcome Scale for Dementia (IPOS-Dem) to detect, monitor and address difficult symptoms. We will interview carers of people with CJD to learn from their experiences. This information will help health and social care professionals improve care towards the end of life.

We are working closely with people with dementia, current and former carers and a representative from the CJD Support Network to ensure our work provides tangible benefits for those living with dementia and CJD. We were invited to the recent CJD Support Network committee meeting and it was great to meet some of the team and discuss our plans.

If you would like to be kept updated about our project, please join our contact list by mailing us at: dop.embedcare@ucl.ac.uk.

Dr Sampson's research team

How you can be involved

We are looking for an expert by experience (a person affected by CJD, either personally or through caring) to join our study reference panel. This is a group of people with early dementia or their family carers and friends who are interested in informing and driving.

For further information please contact us at: dop.embedcare@ucl.ac.uk

Continuing bonds

Reflections on bereavement awareness training

Beth Marsh
CJD Support Network committee member

In May 2016, just six weeks after being told he had sporadic CJD, my dad passed away at the age of 67. Two years on, in May 2018, in my capacity as a CJDSN committee member, I had the opportunity to attend a one-day training course on Bereavement Awareness, run by the charity Cruse. One of the many topics covered was Continuing Bonds theory. I know this may be something many of you are already aware of, but it was new to me and something I felt I would like to share with others who are unfamiliar with it.

In their 1996 book 'Continuing Bonds', Klass and colleagues identify that the purpose of grief is often seen as being to sever the bonds with the deceased in order to free those left behind to 'move on'. I have seen this reflected in my own life in many ways over the past two years; in my own reluctance to put a picture of my dad on my desk at work, in other people's reluctance to ask me questions about my loss. I wonder whether this is something that other members of the network have experienced.

But what if grief is less about 'letting go' and more about re-negotiating our relationships with the person or people we have lost over time? Klass and colleagues argue exactly this. They suggest that healthy resolution of grief means working on and allowing ourselves to maintain a continuing bond with the person who has died. Just as the meaning people have in our lives when they are with us changes over time, so too does the meaning of the person or people we have lost.

So, then, if nurturing a continuing bond with the person we have lost is a healthy way to process and accommodate our loss, the question then is how do we go about it? Klass and colleagues say that 'while death is permanent and unchanging, this process is not' and it's something that we should work on. The key to this, they argue, is through ritual. When I first heard this, I immediately thought of traditional rituals – funerals, burials, scattering ashes, placing flowers at a gravesite – those collective rituals following a death that are embedded in society. The theory of continuing bonds, however, goes further than this. It says that we need to continue to invent, follow and reinvent our own rituals in order to reframe and grow the relationship we have with our lost loved one.

Rituals can be collective or individual. I recently had a conversation with a colleague who was looking forward to attending an annually held mini festival in honour of a friend he had lost, which is organised every year by the friend's mum. A wonderful collective ritual which allows the people who loved him to share together in the things he loved. A personal ritual I have invented since attending the Cruse training is to pick up the London Evening Standard on my way home from work and have a go at the cryptic crossword on the train. My dad was great at cryptic crosswords and always trying to teach me how to do them. It's just a small individual ritual, but it fits into my life and gives me a chance to turn towards a relationship that is changed, not lost.

Turning towards our grief in this way, working on the relationship we have with those we have lost, could be viewed as denial. In fact, the opposite is true. Turning away from our grief, trying to 'move on', avoiding talking about the person at all costs – that sounds a lot like denial to me. Inevitably, acknowledging that our relationship with the person who has died is forever changed requires acknowledgement, also, of the fact that they have died – and this can be so painful. What continuing bonds also allows us to do, however, is to celebrate what the relationship with the person we lost gave and continue to give, to us.

Research grant reports

At an earlier committee meeting of the CJD Support Network, a decision was made to use part of the CJD reserves to provide two research grants of £25,000 each. These were publicised, applications subsequently received and were internationally peer reviewed and evaluated.

The committee agreed to award a grant of £25,000 each, to two research projects by Dr Mok and Dr Nihat.

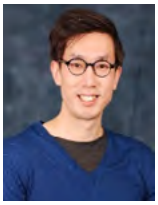
Dr Mok's project relates to issues concerning sporadic CJD, gene mutation and tests on healthy clients, before the disease takes hold. Our funding will enable Dr Mok to purchase a plate reader, an important piece of equipment for his research.

Dr Nihat's project is a feasibility process. It is a computational tool that will include all the data information and use the system of rating clinical aspects to predict key care needs that are going to happen and to predict certain criteria when a client will need 24-hour care. The project is mainly useful for sCJD patients who are already sick.

Dr Mok and Dr Nihat have given their first reports on their work, opposite.

Thank you to all our donors that have ring-fenced their donation for research. This has enabled us to financially support Dr Mok and Dr Nihat with their important research.

Defining the onset of prion infection and neurodegeneration in healthy individuals at risk of prion disease



Dr Tzehow Mok

In the UK, the number of individuals at risk of inherited prion disease is estimated to reach approximately 1,000; in addition, those at risk because of direct medical exposure number many thousands, given that contaminated cadaveric human growth hormone was administered to about 2000 individuals before 1985. The absence to date of a test or biomarker capable of predicting disease onset in at-risk individuals to date has long been recognised as a vital unmet need in the prion disease field. In clinical practice, such a reliable biomarker is crucial in supporting a diagnosis, designing proper clinical trials and in determining the optimum time of starting treatment. It is widely accepted that the chances of achieving a cure are higher the earlier a treatment is administered; an otherwise effective drug may be erroneously dismissed as ineffective as a result of getting the timing of treatment wrong.

Individuals affected by inherited prion disease are usually healthy in the first few decades of life before the symptoms of the illness emerge. To date, there is no way to tell when the disease will start other than by relying on the clinical symptoms, by which time considerable damage to the nervous system has occurred. Similarly to that observed in mouse experiments, we wish to explore if prions emerge and remain at high levels in brains of at-risk individuals for a considerable amount of time before symptoms begin and proteins from injured brain cells leak into the spinal fluid during this clinically silent time. This silent period is a window of opportunity to develop ultrasensitive tests capable of detecting minute amounts of prions and brain proteins in the spinal fluid of the at-risk individuals, both of which may give indications when an at-risk individual might fall ill. In 2016, we conceived a study proposal to collect yearly spinal fluid samples from at-risk groups and to develop these tests, with backing from the UK Alzheimer's Society through a Clinician Training Fellowship in 2017.

Dr Mok's grant allowed the purchase of a microplate reader, used to detect proteins that might help us predict onset of CJD

Pre-symptom testing

Tests to detect brain proteins are already very sophisticated and widely available but tests for prions in inherited disease require further adjustment. The real-time quaking-induced conversion (RT-QuIC) assay which has proved to be extremely useful for sporadic CJD certainly shows great promise in this respect. The RT-QuIC requires the incubation of CSF samples with laboratory-made prion protein and other chemicals, which is repeated shaken vigorously in a microplate reader. A positive reaction occurs when the prions in the CSF sample corrupts the lab-made normal

prion protein to form stacked structures called amyloid which changes the fluorescence pattern of a dye in the mixture detectable by the microplate reader.

We are extremely grateful to the CJDSN for awarding £22,284.75 towards purchasing a state-of-the-art BMG LABTECH FLUOstar Omega Lite microplate reader and three years' Gold and Silver Preventative Maintenance Contract, dedicated for the sole use in this project. This new microplate reader has obviated the need to share with other users, allowing us to perform many more experiments which will critically shorten the time required to hone this technique, specifically for at-risk individuals.

We are actively recruiting at-risk individuals to the National Prion Monitoring Cohort for this important project.

If you have a blood relative affected by inherited prion disease, or if you have been tested positive for a mutation in the prion protein gene and are willing to help with this, please do not hesitate to contact me, Dr Tzehow Mok, at the National Prion Clinic (tel: 0203 448 4037; email: tzehow.mok@nhs.net). You do not have to be tested to be part of this research project.

Prediction of care milestones in Creutzfeldt Jakob Disease

Dr Akin Nihat

Sporadic Creutzfeldt-Jakob Disease (sCJD) is a devastating, progressive illness that affects memory, language, balance, co-ordination and behavior. It's the most common form of prion disease in humans, which are caused by the normal prion protein misfolding and causing damage to the brain and nerve cells. Sporadic CJD is often particularly rapid in its progression and affected patients can change from being independent and well, to being bedbound and unable to communicate in weeks or months. Consequently, patients and their loved ones need dedicated and responsive support from a range of health and social care professionals and local services, often over a very short period of time.

Over several years and with the incredible involvement of over 800 patients and their loved ones, the National Prion Clinic has managed the National Prion Monitoring Cohort (NPMC), an observational study of all forms of prion disease. The aim has been to collect useful information from patients as part of their clinical assessments, to study the natural progression of the conditions in a way never previously achieved.

As a doctor and research fellow working at the National Prion Clinic, part of my role has been to assess and support patients with prion disease and their relatives or loved ones. We have seen that one of the most difficult challenges, particularly in sporadic CJD, is the pace of change in a patient's symptoms and function. Whilst we do our best to offer guidance and advice to local services, it has been unfortunately common for the rate of change in a patient's condition to outstrip the speed at which services can be provided.

Part of the problem is that patients can present and progress in so many different ways that it is incredibly difficult to predict how someone might change and how fast. Our unit has made some important contributions to this issue, both by identifying some factors that contribute to faster or slower disease progression and by creating clinical rating scales that help us to objectively 'score' how far along we think someone's condition is. As part of my work, I have developed two additional scales that we are using to objectively measure how impaired a patient is in their ability to move and think.

All of these tools together have enabled us to build a much clearer picture of how patients progress and provided a huge amount of useful data. We would now like to take the next logical step and ask if we can use this incredible resource to make predictions that will provide patients, their families and supporting healthcare professionals with useful, actionable information to improve patient care planning and quality of life in future.

We will focus on the areas that we have learnt are most important to patients and their loved ones: predicting overall prognosis and estimated time before a patient needs certain levels of care; for example, needing outside care support at home, or 24-hour care. To do this, we will use the data we have collected and a powerful statistical computing technique called machine learning, to develop different predictive models and test their ability to correctly forecast these milestones. Ultimately, we plan to make this data available in an appropriate format to patients, loved ones and healthcare professionals to assist with service and care planning and address this profound unmet need for our patients.

Refurbished Courtauld Building, new home for the MRC Prion Unit

The Medical Research Council (MRC) Prion Unit at University College London (UCL)

Professor Simon Mead

The Medical Research Council (MRC) Prion Unit at University College London (UCL) recently moved to newly refurbished premises, The Courtauld Building, 33 Cleveland Street, London, in Fitzrovia near the BT Tower.

Previously unoccupied for over ten years, The Courtauld Building was comprehensively remodeled internally to create new laboratories, meeting rooms, office and social space. The work was funded by UCL and MRC to help facilitate a long-term partnership to advance understanding of the fundamental mechanisms of prion and other neurodegenerative diseases to find groundbreaking treatments for patients. The building also houses the offices of University College London Hospitals NHS Foundation Trust's National Prion Clinic. We are fortunate that the National Hospital for Neurology have an adjacent out-patient facility on Cleveland Street where we can see patients who are able to travel to London. The co-location of these clinical and research functions allows doctors to integrate closely with basic scientists, enriching both disciplines.

The work done to refurbish the building was extensive as it had fallen into considerable dereliction. The tasks included replacing the rear 1980s façade, providing a new main entrance and relocating it to Cleveland Street, renewing the roof and fifth floor, a new reception area and office space, a new flexible meeting room / lecture theatre area, new research laboratories, including facilities that can handle human and bovine spongiform encephalopathy prions, new research support rooms for microscopes and freezers. The lift shafts and stairwell were repositioned to create a more open plan and efficient area to better serve the research needs.

The Courtauld Building is not new to medical research. It was opened as the Courtauld Institute of Biochemistry for the Middlesex Hospital Medical School in June 1928, with the founding stone laid in 1927. Funding was donated by Mr Samuel A Courtauld with additional sums for the Chair (professor) of Biochemistry to the extent of £20,000 and a further £20,000 (total equivalent to £2.4 million in 2019) to support the running of the Institute. The main initial purpose was to provide all the routine clinical biochemical tests that were needed by the Middlesex Hospital. Basic research was also done at the Institute, with particularly remembered researchers including Frank Dickens FRS, who described the pentose phosphate pathway and its relationship with tumour growth; Edward Charles Dodd's FRS, who was Director of the Institute for forty years and also researched cancer, food and diet; and Sir Brian Wellingham Windeyer FRCS who was an early pioneer of x-ray and radium treatment for cancer. The Middlesex Hospital closed in

2005. After a pause, the MRC Prion Unit at UCL now picks up the baton of medical science discovery at the Institute.

The benefactor for the original building, Samuel Augustine Courtauld (7 May 1876 to 1 December 1947), is recognised by a plaque at the entrance to Institute. He was a businessman who made his wealth from the development and sale of fabrics, clothing, artificial alternatives to natural fibres like silk and chemicals. Courtaulds plc and Courtaulds Textiles Ltd. were major British companies, which were eventually broken up and sold in 2000-2006. The latter company was predominantly staffed by women and manufactured ladies' underwear, owing brands Gossard and Pretty Polly. Mr. Courtauld is probably best known however for his patronage of the arts, including the founding of the Courtauld Institute of Art in 1932 and bequeathed his art collection to the Institute of Art when he died.

The Prion Unit is one of the world's leading research centres and is the sole occupant of the building for the purpose of studying prions and degenerative diseases of the brain more generally. The Unit has a long-term research strategy in prion diseases such as Creutzfeldt-Jakob disease (CJD) and has interests in studying the connections and relevance of the disorders to other much commoner causes of dementia such as Alzheimer's disease. We look forward to welcoming members of the CJD Support Network to our new facilities at joint Open Days of the MRC Prion Unit at UCL and National Prion Clinic.

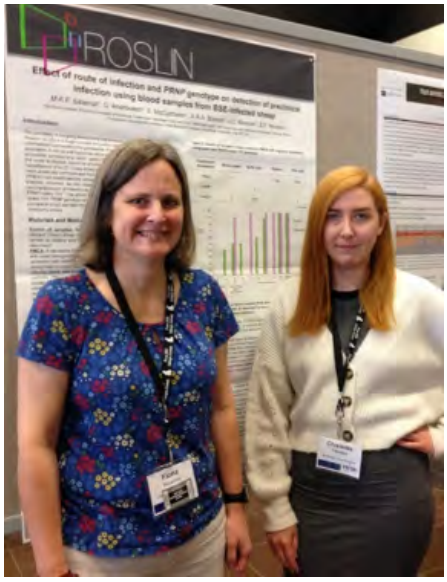
See www.prion.ucl.ac.uk/clinic-services/forthcoming-events/

Developing diagnostic tests for subclinical vCJD

Charlotte Thomas and Fiona Houston
The Roslin Institute, University of Edinburgh

Introduction

A laboratory test for variant Creutzfeldt-Jakob disease (vCJD) that can accurately detect the disease at an early stage of infection (long before an affected individual becomes ill) could potentially be of great benefit in protecting the public from further spread of the disease. Ideally, this test should be able to work on patient samples that are non-invasive and easy to collect, such as blood or urine. Such a test could be used for early diagnosis, or to screen donated blood for vCJD. It could also help us to identify 'carriers' of the disease, who might be at risk of infecting others. This article outlines our plans to develop a blood test for early detection of BSE infection in sheep. If successful, this test could then be adapted for use in humans.



Charlotte Thomas and Fiona Houston

Background

The link between the cattle disease, bovine spongiform encephalopathy (BSE) and vCJD in humans is well known. However, despite estimations that many thousands of people were potentially exposed to BSE-contaminated food following the large BSE outbreak of the 1980s/1990s, only 178 cases of vCJD have been identified in the UK to date. The reason for this discrepancy is not fully understood. One likely (and reassuring) explanation is that the transmission of animal prions to humans is highly inefficient. On the other hand, individuals infected with prions can remain healthy for up to several decades before developing signs of brain disease. Therefore, although the number of new vCJD cases has decreased considerably in recent years, with no known living cases in the world at this point, further individual cases are expected and a second wave of cases might still be on the horizon.

In addition, studies of appendix samples surgically removed from otherwise healthy patients suggest that a small percentage of the UK population may be carrying vCJD without showing any outward signs of disease. Although there is some uncertainty about the interpretation of these studies, it is possible that these individuals are at risk of infecting others, e.g. through blood or organ donation. Indeed, there have been several cases of vCJD traced back to exposure to infected blood.

Currently, there are no diagnostic tests which can easily identify

individuals with these 'silent' vCJD infections (also known as subclinical infections). Several blood tests have been developed which can accurately identify patients with clinical (symptomatic) vCJD, with one test identifying subclinical infection. However, these tests have been evaluated on only a limited number of samples.

With funding from the UK Department of Health, the aim of our research is to identify which (if any) of these tests are best able to detect prion infection before the signs of brain disease appear.

An animal model of vCJD infection

All past cases of vCJD were diagnosed following the onset of clinical symptoms; as a result, there are very small number of blood samples available that were collected during the silent subclinical phase of infection. Previously, we have used sheep infected experimentally with BSE to study the risk of transmitting prion diseases by transfusion of blood components commonly used in humans. Sheep were used for these studies because they show many similarities to human vCJD patients when they are infected with BSE and are a similar size to humans. Blood samples from infected sheep were collected and frozen at regular intervals, from the time they were infected until they developed signs of brain disease 2-4 years later. Thus, in the absence of suitable human samples, we intend to use these sheep blood samples to find out which diagnostic tests are best at detecting subclinical infection.

Diagnostic tests

Prion diseases are thought to be caused by the build-up of a misfolded protein (called 'prion protein', or PrP) in the brain, resulting in damage and death of brain cells. The most specific diagnostic tests for prion diseases rely on detection of misfolded PrP, but efforts to develop tests for readily accessible samples, such as blood and urine, are hampered by the tiny quantities of the protein found in these samples.

Recently, a new generation of laboratory tests, known as 'prion amplification assays', have been developed to overcome this issue. These methods work by amplifying the amount of misfolded PrP to a level that can be readily detected by standard laboratory procedures. We are currently adapting these tests for detection of misfolded PrP in our BSE-infected sheep blood samples.

Progress to date

We currently have prototype versions of two prion amplification assays, called 'protein misfolding cyclic amplification' (PMCA) and 'real-time quaking induced conversion' (RT-QuIC) set up in our lab. Both platforms give very sensitive detection of misfolded PrP in sheep's blood. The next step is to find out which test (if any) performs best in detecting subclinical infection. The most accurate and sensitive blood test(s) can then be taken forward for use in humans.

In conclusion, a laboratory test for subclinical vCJD would be of enormous benefit for public health protection. It could be used to screen blood and organ donors and could function as an alternative approach to large-scale appendix surveys, allowing us to estimate the level of silent vCJD infections in the UK population. The outcomes of our study will also help us to better understand the risks of human-to-human transmission and devise measures to minimise those risks.

CJD Support Network Raffle

2019 sees the first ever raffle organised by the CJD Support Network. The prizes are great and all the profits will go towards the cost of the Family Support Meeting.

We have included a book of raffle tickets with the Newsletter. We would be very grateful if you could sell some tickets to your family and friends. If you need more tickets, please contact the Network.

Promoter: CJD Support Network, PO Box 346, Market Drayton TF9 4WN. The CJD Support Network is the leading UK care and support charity for all forms of CJD. We welcome public donations to support us in our work. Registered Charity Number 1097173

Prizes

- **A Portrait of the Winner** – painted by Diane Louise Newell, international artist.
- **A Crystal Head of Vodka** – the Rolling Stones 50th anniversary commemorative pack, 70cl.
- **Gin in a basket** – two litre bottles of gin, a range of tonics, a few small bottles of gin, a box of gin spices, all gin-themed and attractively parcelled.
- **Two tickets for the Tottenham Hotspur home Premier League game against Norwich City** on 22 January 2020.
- **£100 cheque** – donated by Bob & Marie Kassai

Fundraising news

My beloved mum

Diane Manns

We lost my beloved mum Diane Manns to sporadic CJD on 14 November 2018. She was 62 years old and prior to symptoms she was extremely active, loved her garden and being with her grandchildren and family.

Her symptoms started in May 2018, when she complained of a frozen shoulder and, shortly after, ringing in her ears (tinnitus). By June she was unsteady on her feet and come August bank holiday weekend she started to lose her memory and she had a couple of falls.

Mum was finally admitted to hospital in September, after her GP became concerned about the sudden memory loss and falls. The consultant at the hospital told us he suspected CJD and a series of tests were carried out. A specialist team from Edinburgh came down to meet Mum and diagnosed CJD. Mum was then released for palliative care.

Mum lived out her final weeks at home, cared for by her amazing partner and supported by the family. Deterioration was rapid, week-on-week. Each week we would notice another debilitating decline and this soon became the new 'normal'. From complete memory loss to being completely unable to talk and communicate (and my mum was a talker) to finally becoming completely confined to armchair/bed, as she had lost the use of her legs. However, everyday her partner washed and dressed her. I know this sounds simple, but by this point the effort involved in doing this every day by himself was huge! In some ways just this small act made things appear normal, as Mum always looked like Mum. Swallowing soon became a problem, then consuming food and drinking water.

Within days Mum passed away, at home surrounded by her loved ones, exactly eight weeks after her diagnosis.

Kelly Maggs (Diane's daughter)

Network stylus pens!

To raise money for the Network we are selling CJD Support Network branded ball point pens with a stylus end which you can use on a tablet or smart phone. These useful pens cost £2 plus p&p each and you can buy them by contacting the Network at the address on the back page.

Mick's Baby Girl

Mick's Baby Girl

Mick and Annette

My late husband Mick loved his greyhound racing. He was also a kennel hand – I still have his retired dog at home with me. Our dear friends Martin and Carol, who are greyhound trainers, have bred a greyhound and in memory of Mick her racing name is 'Mick's Baby Girl'. She runs at Doncaster Greyhound Stadium and is trained by Martin Haythorne. At Martin's request any money received from running (run money) will be donated to the CJD Support Network.

Annette Beal

London Marathon runners 2019

Paulina Sutton and John Barrett both ran the London Marathon in aid of the CJD Support Network on April 28 this year. We are most grateful to them and to the many people who gave through the Just Giving website.

It is not too late to donate! See the Latest News page on our website www.cjdsupport.net for the links to Just Giving.

Paulina Sutton

It was great fun training for London Marathon and supporting a charity close to my heart. One in 10 people get to the London Marathon through the ballot, so when I signed up I didn't have big hopes.

However, in October, I received a letter with confirmation of my place and immediately knew I would like to open my own fund-raising page even though I didn't have to fundraise to get a place.

My biggest aim for fundraising the money for CJD, was to raise as much money as I could, so one day someone doesn't have to suffer like myself from the loss of their closest person. I'm full of hope that one day cure will be found for this sad and horrible disease.

I opened my Just Giving page in October, giving myself a target of £1,300. I started posting about my page on Facebook and Instagram and within the first two months I had received £450 from my friends and clients.

I'm a triathlon coach and personal trainer, so I planned my own training programme. I started my training in January 2019 aiming to run three times a week, with some recovery weeks when I did some cycling instead of running. I also went to Lanzarote to coach at a couple of training camps and had good opportunities of training whilst coaching.

Training for the marathon wasn't easy, as my work, allotment and college take most of my time, but even with missing some training sessions, I knew I'll complete the marathon – if I had to walk it!

When training was getting tough my motivation was my mum, who passed away from CJD in summer 2017. In the past I had taken part in Ironman Triathlons and my mum was my biggest supporter, so when training was tough I knew she was looking at me, smiling like she always did when I finished my long-distance events.

Midway through my training I also received my CJD Support Network T-shirt which I took to my local running club to print my and my mum's name on it and a couple of pictures of us together. I knew I would like to have mum with me on the day, so I planned to wear the CJD Support Network T-shirt on the day of the marathon.

As the event was getting closer, I started receiving more donations and three weeks before race day I was only £5 short of achieving my target. This was quickly achieved and in the end, I received far more donations, eventually raising 118% of my target.

The day of the Marathon came quickly and I was looking forward to completing what I had been training for in the last six months. I booked myself on a 6am coach from Milton Keynes to the London and the marathon start line. The weather couldn't have been better, it was cloudy with a light breeze.

My start was at 10:40 so I didn't have to wait very long. When I started running, for the first 10–15 minutes I tried to settle into a nice comfortable running pace and enjoy the crowds, but suddenly something hit me and I just couldn't stop crying.

All memories of mum came back and I then realised how much I have missed her. I had to stop and walk for a bit and calm myself down. It is very crowded in London, so I felt very anxious that people were looking at me crying, but eventually I managed to get back into my pace and ran comfortably until halfway.

When I ran onto London Bridge, which was the halfway point, I had a very bad stitch in my stomach and decided to slow down a bit. After 15-20 minutes, I was able

to start running again, but kept stopping and hugging people who came to watch and support me. I ran and walked for the last six miles of the race, but I never had any doubts about finishing. I knew I would complete it no matter what, and do it for my mum.

I managed to finish in four hours and six minutes. Recovery took me a good couple of weeks and now, a couple of months afterwards, I'm back to running shorter distances again.

Paulina Sutton

John Barrett

John's sister-in-law Catherine Francke died of sporadic CJD

I ran the London Marathon on 28 April 2019! Though this was my third London Marathon and my fifth marathon. It's seven years since my last run at this crazy distance – it was tough!

However, I did this for a great cause. It is with much sadness that my wife lost a truly wonderful person, her sister Catherine, who very sadly became ill with Sporadic CJD, only diagnosed last year and just 51 years old. Catherine's death left her dear husband, two wonderful sons, a dear brother, my dear wife and Cath's other dear sister – and of course many friends and other family – devastated.

It was so painful seeing her and the family suffer, with this quite devastating illness. It was truly heart-breaking. Catherine and the family battled till the last, when she sadly could hold on no more.

But she left us with such dignity and grace. It was peaceful, with the family there with her. I'm so sad just writing this, but happy that her suffering is no more and she is now at peace.

With the cause unknown for this form of CJD, there desperately needs to be research done and ongoing support for sufferers, family, friends and anyone connected with this dreadful illness.

The CJD Support network offers this much needed support. So, for me and all who knew Catherine, I've no hesitation trying to raise money for this very worthwhile charity. Hoping that one day their help (your help) can find a cure, but until then, give the much-needed support sufferers and family need at this very traumatic time in their lives.

Donations in memory

Our heartfelt thanks to the families and friends of those below, for donations received in their memory by the CJD Support Network, between May 2018 and June 2019.

Mr A R Baker
Kevin Barker
Emma Sara Broughton
Rita Ann Brown
Frederick Ron Burnett (Ron)
Christine (Tina) Caster
Chris Collins
Pat Conlon
Martin Dee
Danny Doherty
Barbara Janet Earl
Janet Ellis
Tony Escritt
Linda Fanning
Catherine Francke
Manugouri Galoria
Christopher Gaukroger
Christine Hills
Joanne Hodgson
Robert Hoehr
Massar Ji
Diane Jones
Margaret Jones
Wynford Jones
Michael Gerrard Kiely
Roger Lovell
Diane Manns
Daniel Matthews
Clive Morgan
Brian Morrissey
Janet Oakley
Philip Osbourne
Penny Rennie
John Saunders
Dorothy Jennie Scott
Ian Scott
Piara Singh
Mike Smitten
Czeslaw Szymczak
Alan Tittensor
Alan Williams
Mary Wearing

Management Committee 2018–2019

Professor Richard Knight, Chair Richard is a Clinical Neurologist at the National CJD Research and Surveillance Unit in Edinburgh.

Professor Simon Mead
Simon is a neurologist working at the National Prion Clinic.

Gillian Turner
National CJD Support Network Co-ordinator

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

Annette Beal
Annette works in a care home. She lost her husband to sCJD in May 2017.

Kate Dahill
Kate works as a junior doctor. She lost her aunt to sCJD in 2012

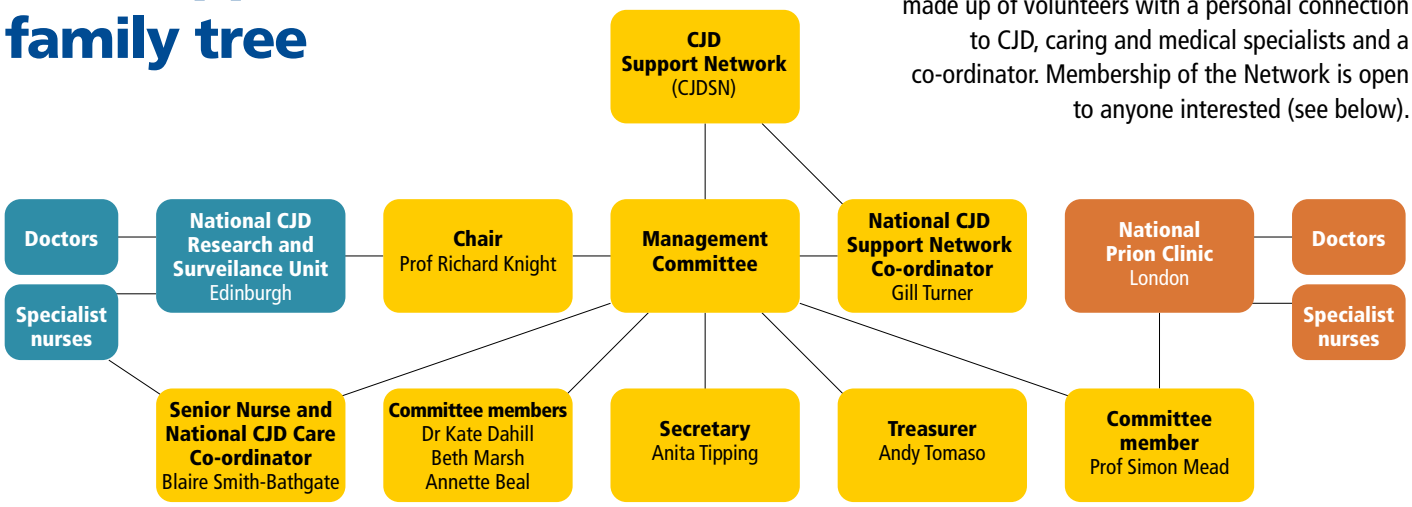
Andy Tomaso, Treasurer
Andy lost his mother to genetic CJD in 2007.

Beth Marsh
Beth works in psychopharmacology. She lost her father to sCJD in 2016 and joined to support young people.

Blaire Smith-Bathgate
Blaire is a National Care Co-ordinator and Senior Nurse at the National CJD Research and Surveillance Unit in Edinburgh.

CJD Support Network family tree

The Management Committee of the Network is made up of volunteers with a personal connection to CJD, caring and medical specialists and a co-ordinator. Membership of the Network is open to anyone interested (see below).



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

☐ Please tick to agree to us keeping this information on file. We need this to contact you and will never give it to a third party except with your explicit consent.

Contact: Gillian Turner, CJD Support Network, PO Box 346, Market Drayton TF9 4WN
Telephone 0800 0853527 · Email gturner@cjdsupport.net · Website www.cjdsupport.net

Charity number 1097173