

GOOD NEWS

Blood test offers hope for earlier diagnosis

Health news in the the *Daily Mail* online 13 October 2004 reported that a new blood test, developed by Proteome Sciences, a company specialising in protein research, could be widely available within twelve months. Proteome Sciences are working with the CJD Surveillance Unit on the test which is devised to target specific protein changes in blood which will allow doctors to diagnose vCJD years ahead of a patient developing symptoms.

Infection control

The *Journal of General Virology* (2005) 86, 869-878 described research by Professor John Collinge et al at the MRC Prion Unit detailing 'an enzyme-detergent method for effective prion decontamination of surgical steel'.

Effective sterilization procedures for surgical instruments to protect transmission of CJD and other prion diseases have been a concern and a high priority for the Department of Health.

The research showed that the prion-degrading reagents identified in the study are readily available, inexpensive, non-corrosive to instruments, non-hazardous to staff and compatible with current equipment and procedures used in hospital sterilization units.

Successful 'Meet the Expert' family support meeting

To celebrate International CJD Day on 12 November, the CJD Support Network arranged a very successful 'Meet the Expert' family support meeting on Saturday 13 November.

The meeting was held at the Westminster Quality Hotel, London. Although the attendance from members was disappointing, for those who did go, the access to CJD experts – to ask those burning questions that they did not have the opportunity to ask previously – was much appreciated by families.

Amongst the experts available to answer the questions were; Dr John Stephenson, Chief Research Officer at the Department of Health, Dr Daffydd Thomas, consultant neurologist and Clinical Trial Co-ordinator at the MRC Prion Unit, Patricia Hewitt, lead consultant in transfusional microbiology at the National Blood Service, Katie Oakley, CJD incidents nurse investigator at the Health Protection Agency, Dr Andrew Smith, microbiologist at Glasgow Dental School, and Lester Firkins, a father who lost his son through vCJD but who now works at the Medical Research Council.

Families were invited to circulate round the room of tables, each hosted by an expert, to ask their questions and discuss any issues of concern.

On Sunday 14 November in the chapel at Chelsea and Westminster Hospital, London, a remembrance service was held for loved ones who had died with CJD.

This was a very moving service. A memorial role with thirty names was read out and candles lit in their memory. Dr Angus Kennedy, consultant neurologist and Chairman of the CJD Support Network, gave a very memorable address. After the service, Angus treated the congregation to coffee in the hospital café.

We were very pleased with the arrangements for this special weekend and hope that more of you will join us in a similar event in October 2005. If you have any ideas for future events that you would like us to arrange, please contact Gillian Turner.

ON OTHER PAGES

- 2 News
- 3 Support for each strain of CJD
- 4 Genes may determine type of CJD
- 5 Letters
- 6 Q&A: CJD risk factors study
- 8 Dept of Health research strategy
- 10 PRION-1 drug trial
- 12 Who's who in CJD

Staff changes

National CJD Surveillance Unit

Care co-ordinators at the National CJD Surveillance Unit, **Gordon McLean** and **Fiona Barnett**, have both left for new roles elsewhere. Gordon will be working in cancer services in the South East of Scotland. Fiona has taken a post as clinical nurse specialist for multiple sclerosis in Nottingham. We thank them for all their hard work over the past few years and wish them every success in the future.

As we say goodbye to this duo, we are very pleased to welcome **Margaret Leitch** the new care co-ordinator.



Margaret Leitch Before joining the Unit as a research nurse, Margaret was a community psychiatric nursing sister in South Wales, so she is well able to fill the empty shoes.

National Prion Unit

At the end of 2004, the National Prion Unit moved from St Mary's Hospital, Paddington to a new home at the National Hospital for Neurology and Neurosurgery, Queen Square, London.

Dr Dafydd Thomas, consultant neurologist and clinical co-ordinator for the CJD treatment trial has now left the Prion Unit and has been replaced by **Dr Stephen Wroe**. We would like to thank Dafydd for the support he has given to the CJDSN and for the steady influence he has had in bringing the clinical trials to fruition. We welcome Dr Wroe and look forward to working with him in the future.



Dr Stephen Wroe

Good news in palliative care

As from the 1 November 2004 the National Council for Hospice and Specialist Palliative Care Services will be known as the National Council for Palliative Care.

This change of name and redefinition of their remit, will allow them to encompass the whole spectrum of palliative care across all diagnoses and in all settings. This is good news for future patients and families affected by any strain of CJD.

For further information on the National Council for Palliative Care their contact details are enquiries@hospice-spc-council.org.uk or their website at www.hospice-spc-council.org.uk or telephone number 020 7520 8299.

Government to change BSE Controls

On the 1 December 2004 the Government announced the start of a managed transition towards the lifting of the 'over 30 month rule' and its replacement with a system of robust testing of cattle for BSE. This rule currently imposes an automatic ban on older cattle from entering the human food chain.

However, they confirmed that the main public health protection measure – the removal of specified risk material (SRM), which is estimated to remove over 99% of infectivity in cattle – has been

and will continue to be rigorously enforced by the Meat Hygiene Service.

The statement said that the incidence of BSE has been declining since its peak in 1992 and has now fallen by over 99%. The numbers of new clinical cases detected are also at the lowest level since recording began.

Editor's comment: The Food Standards Agency reported in August 2004 that the Meat Hygiene Service had discovered a failure to remove SRM from bovine carcasses at a small red meat plant in Scotland. They found seven carcasses containing thymus tissue (SRM) in the neck area. Further investigation found a further four carcasses contained thymus and one also contained spinal cord. One carcass had been sold by the operator to a local butcher. It was possible that this carcass may also have contained thymus tissue, but there was no evidence to confirm this. For further information www.food.gov.uk/bse/bsearchive/202.

Early diagnosis issues conference

As a blood test is hoped to be available within the next few years for CJD, at the request of the Chief Medical Officer, the Health Protection Agency arranged a small conference with selected invited delegates in March 2005, to discuss the social and ethical issues around informing future patients that they are at risk of developing CJD.

Recent CJD figures

The number of deaths of definite and probable cases in the UK, up to 4 March 2005, from the CJD Surveillance Unit in Edinburgh.

Year	Sporadic	iatrogenic	Familial	GSS	vCJD	Total*
2003	77	5	4	2	18	106
2004	47	1	2	1	9	60
2005	5	0	0	1	1	7

Total deaths to 4 March 2005: 1027

*As at 4 March 2005

Fundraising news

Fun run *Anita Tipping*

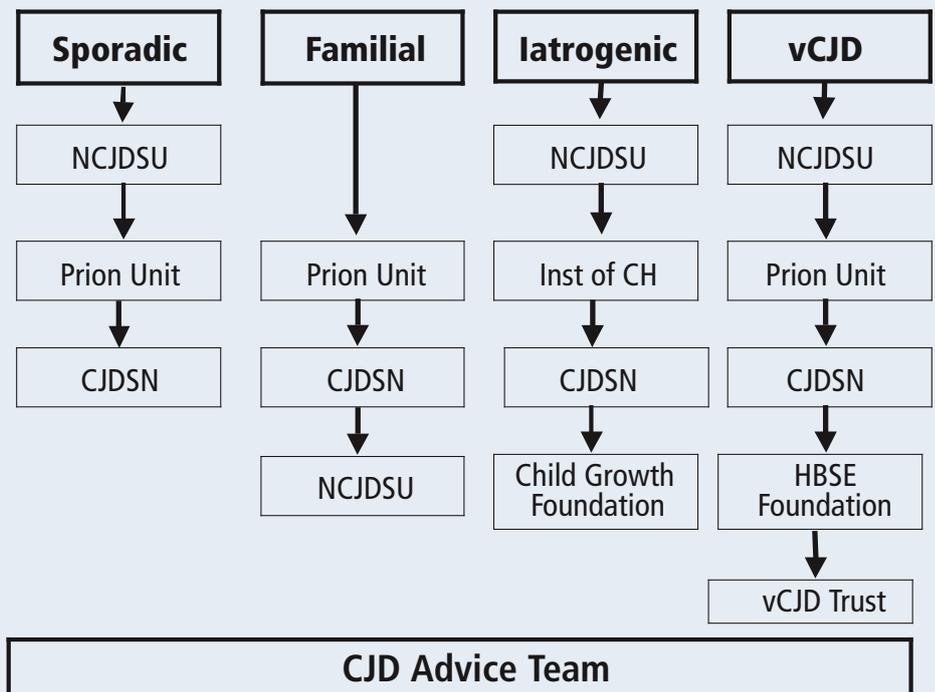
It was a bright, sunny day one Sunday in September last year when I did a fun run in Hyde Park. The place was crowded with runners and supporters of all ages representing individual charities. Being there and seeing everyone giving themselves to help others humbles you. One thing that will be with me forever will be that I really enjoyed the run as I normally hate running and have never run before. I shall be running again this year and anyone who is interested to join me will be most welcome. You will enjoy it, guaranteed!

Thanks to everyone who supported me and gave so generously.

Dance night

Tracy Huggetts, whose father died of sporadic CJD, arranged for Brighton's rising stars Lady Marmalade to provide their services free, and persuaded the owners of a trendy bar in Springfields, London, to provide the use of The Gate free for a night. This explosive seven-piece covers band played chart classics from the 60s to present day. From 'Carwash' to Kylie, Lady Marmalade filled the dance-floor throughout the night. The band consisted of three distinctive and dynamic female vocalists and a back-line of live keyboards, guitar, bass and drums. Their lively show was complemented by funky costume changes and an exciting stage performance. A good night was enjoyed by all who attended.

Supporting organisations for each strain of CJD



Contact details

National CJD Surveillance Unit (NCJDSU)

Western General Hospital
Crewe Road
Edinburgh EH4 2XU
Telephone: 0131 537 3073
Website: www.cjd.ed.ac
Care co-ordinator:
Margaret Leitch 0131 537 3073
www.cjd.ed.ac/uk/care.html

National Prion Clinic (Prion Unit)

National Hospital for Neurology and Neurosurgery
Queen Square
London WC1N 3BG
Telephone: 0207 061 9880
Email: Prion.help@hclh.org
Website: www.nationalprionclinic.org

Institute of Child Health

Contact: Leah Davidson
020 7242 9789
39 Guildford Street
London WC1N 1EH

Human BSE Foundation (HBSEF)

Chairman: Janet Gibbs
Secretary: Frances Hall
Helpline: 0191 389 4157
Website: www.hbsef.org

CJD Support Network (CJDSN)

Contact:
Network Co-ordinator, Gillian Turner
Helpline: 01630 673973
Website: www.cjdsupport.net

vCJD Trust

Compensation scheme for vCJD families
Charles Russell Solicitors
Contact: Edwina Rawson
0207 203 8838

CJD Advice Team

Volunteers drawn from occupational therapists, physiotherapists, district nurses, social workers, patient support representatives and other members of the multi disciplinary team.
Contact in the first instance can be made through the CJD Support Network, HBSE Foundation or the National CJD Surveillance Unit, care co-ordinator.

Genetic make-up may determine what type of CJD occurs when humans are infected with BSE

New research published by a team from the Medical Research Council (MRC) Prion Unit offers an explanation as to why only people with a particular genetic make-up have so far developed vCJD. It also provides evidence that other types of BSE-derived prion infection with a different pattern of symptoms might occur in humans. The findings are published in the journal *Science*.

Variant CJD (vCJD) is the human disease thought to be caused by eating food contaminated with the infectious agent, known as a prion, responsible for the epidemic of BSE or 'mad cow disease' in cattle. So far, everyone known to have developed vCJD has been of a particular genetic type known as MM. Until now it has been a mystery why everyone that has developed vCJD is of the MM type and one possibility is that they are simply the first to develop the disease when infected with BSE, and that people with the other genetic types (known as VV and MV*) infected with BSE prions will

also develop vCJD, but some years later.

In a series of experiments spanning more than ten years, the MRC team has been studying mice genetically modified so that they make human prion proteins, which are used to model human susceptibility to BSE. The team has now shown that mice with the human VV genetic type do become infected when given BSE or vCJD prions, but manifest a different form of the disease which looks quite different to vCJD and has a novel prion 'strain' type.

Remarkably, when these novel prions were used to infect mice of the MM genetic type, the mice either developed a disease very like vCJD, or else a pattern of disease that looks like so-called sporadic CJD – the 'classical' form of CJD. This form has been known about for many years, is seen all over the world and has not hitherto been associated with BSE. However, the new strain identified in the mice, being called 'type 5', has not been seen yet in people and we do not know what pattern of disease it would cause. It could look like one of the forms of classical or sporadic CJD or perhaps be yet another different 'variant' form.

The work from the MRC team suggests that type 4 prions, the type associated with vCJD, can only propagate themselves in people that make the M form of the protein. It seems the V form of the protein just cannot adopt the particular molecular shape that characterises type 4.

The studies in mice also suggest that if these prions were to pass from person to person (for example by blood transfusion) then, depending on the genetic type of the person becoming infected, at least three different patterns of disease might result: type 2 (which is seen in sporadic CJD); type 4 (which causes vCJD) or type 5 (which may cause a new pattern of disease).

Professor John Collinge, Director of the MRC Prion Unit, which is based at University College London, said: 'These mouse studies give us vital clues about the behaviour of prions and how they appear to modify and adapt depending on the genetic makeup of the individual they are infecting.

'We always have to be cautious about making direct comparison to the human condition, but our work strongly suggests that we cannot assume only those with one genetic profile are vulnerable to BSE infection.

'At this stage it is not possible to say how this should alter estimates of those likely to become ill, but our findings do suggest we should be taking steps to draw up a more sophisticated system of categorizing the disease so that we don't mistake BSE related infection for a version of sporadic CJD.'

Human Prion Protein v129 prevents expression of vCJD phenotype.
Journal Science Vol 306, page 1793
– 1796

*The human prion protein comes in two common forms, known as M and V. Because everyone has two copies of this gene, there are three possible genetic types: MM, MV and VV.

Strains of prions

Prions are rogue forms of one of the body's own proteins – known as the prion protein – which are misshapen. There are several different rogue or misshapen forms that can infect humans, and these different types of prions are known as 'strains'. This is analogous to different strains of other germs such 'flu virus causing influenza or strains of salmonella causing different forms of food poisoning for example.

The strain of prion causing vCJD is known as type 4. Types 1-3 cause the different forms of sporadic or classical CJD. Each strain causes a different pattern or type of disease. It is known that prion strains can change or 'mutate' when they pass between different animals.

Dentistry

Dear Editor,

I thought your readers might be interested to hear about the continued frustration I have experienced with my dentist as a result of having the inherited gene of CJD, and the problems caused by this.

It was in May of 2000, that I finally had to write to my MP Mr Alan Hurst (Labour). My NHS dentist of over 20 years had refused to treat me any more, as I had confirmed to him that I carried this gene. After nine months of being without a dentist and in pain for part of this time, with the intervention of the MP, I was allocated a local NHS dentist. The local health authority, brought me my own dentistry equipment, at a cost of £8,000, so I was informed.

I was under this dentist for nearly two years. The relationship was always a bit strained, as appointments were often cancelled at short notice. In fairness, this dentist worked alone and was very busy. So it was with some relief that without warning I was then transferred under the local authority's PCT section to the special needs unit. I am disabled with multiple sclerosis and diabetic, so I qualified for this section.

At my time of transfer to this unit in December 2002, I was complaining of toothache from the lower right hand side of my mouth. For a year, possible causes for the pain were eliminated. As my dentist (who was head of the unit) told me she was only capable and confident to do root treatment on front teeth, she agreed to refer me to a specialist for possible root filling in my back teeth. This is where the NHS system grinds to a halt. After a lot of chasing of correspondence, by myself and the Prion Unit, I was referred to the dentistry school at the Royal London Hospital. This was the nearest place to Essex that had a NHS root specialist! I was seen here twice. On the second

visit some four months later, and after a total of six hours at the dentistry school, with several people poking around in my mouth, yet nothing being done, it was agreed that I should be referred to a root specialist. The wait was to be between six months and three years. Faced with more delays and in considerable pain, which had now gone on for over sixteen months, I approached several private dentists, all of whom would not touch me because of their paranoia over CJD. Finally my husband's private dentist, who had become aware of my growing problem, intervened and in April of 2004 took just half an hour to relieve me of my initial pain by completing a full root treatment on one of the two teeth in question.

I contacted my MP Alan Hurst again in March 2004, to highlight the continuing problems I was having. I asked him to raise several questions on my behalf, with the right government departments. Why is that a special needs unit does not have a root specialist that they can call upon when needed, either from private or public sources? Why is that the government's policy of buying in services from other hospitals does not appear to cover dentistry? Why is that the CJD fund does not cover costs for private treatment where the NHS system cannot provide prompt treatment? At the time of writing this article I have still not had a reply from my MP.

I do not write this article to be malicious and a troublemaker. I feel I am being treated like a modern day leper through no fault of my own, because of CJD. I have always been open and honest about my condition when coming into contact with any medical person. But this has only caused me hassle and anguish at the delays in treatment. I do believe STRONGLY that more has to be done to respond to everyday situations of medical problems with the implications of CJD, either through the special

fund having its parameters broadened, or through more experts being 'on call' to the Prion Unit when needed.

Sarah Ridgewell

Postscript

Sarah has now received a reply from Minister of State, Rosie Winterton MP. The CJD Support Network are very disappointed to read that she writes 'Mrs Ridgewell also asks if the Department of Health can reimburse her for the cost of private dental treatment using the CJD fund. The CJD fund was established only for those with vCJD and their families and is not available to those with the inherited form of the condition'.

The CJD Support Network have taken up this matter on Sarah's behalf and have written to Rosie Winterton pointing out her mistake and emphasising that the National CJD Care Package is accessible by all strains of CJD. We are still waiting for the Minister's reply.

'Meet the Expert' family support meeting

I would like to say a big thank you for the 'Meet the Expert' family support meeting held on Saturday 13 November. It was very informative. I was very impressed with the access I was given to such eminent experts.

Michael Bradley

Thank you for organising such a successful meeting at Eccleston Square on Saturday 13 November. I enjoyed it immensely and found it very helpful. I was surprised on our 'therapy table' that there was so much interest in the pathology!

Dr D J Thomas

I really enjoyed attending the meeting in London
Dr John Stephenson
Chief Research Officer
Department of Health

The case control study of risk factors for Creutzfeldt-Jakob disease in the UK

Some of your questions answered

Dr Hester Ward – National CJD Surveillance Unit

Q What is a case control study?

A A case-control study is one way of trying to find out about the causes of a particular disease – often referred to as ‘risk factors’. They involve collecting information that might be important for the disease from people with the disease (‘cases’). Similar information is collected from a sample of the general population, called ‘controls’. The information collected from cases is compared with that from controls to see if cases were more or less likely to have been exposed to a particular factor. For example, if people with heart disease were more likely to smoke than controls, it suggests that smoking may be a risk factor for heart disease.

Q Why perform a case control study of CJD?

A For variant CJD, it has been suggested that the most likely way that humans were infected was through eating beef and beef products. This is very plausible, but has not been ‘proved’. The recent probable transmission of vCJD by blood transfusion is a reminder that we cannot assume that all people with vCJD were infected by diet. We are performing a case-control study of risk factors for vCJD to try to clarify to what extent people with CJD were infected through diet and to identify in which other ways, if any, people were infected. We also remain very uncertain of the ‘causes’ of sporadic CJD and so we are conducting a study of sporadic CJD to see whether there are any risk factors that mean some people are more likely to develop the disease than others.

Q We know that vCJD came from eating beef, so why do you need to do a study?

A Although it seems likely that eating beef products was the cause of most cases of people with vCJD, it is still important to try and confirm this scientifically. For example, it is important to understand how vCJD can be transmitted so that government policy can be developed and implemented to prevent onward transmission in this and other countries. It may also help in the development of diagnostic tests and treatment for CJD.

Q Who is co-ordinating this study in the UK?

A The National CJD Surveillance Unit in Edinburgh (www.cjd.ed.ac.uk) has been carrying out a case control study of risk factors for sporadic CJD since 1990 and for variant CJD since it was first diagnosed in 1996. This is done in collaboration with those with CJD and their families, controls and their families, clinical colleagues throughout the UK and academic colleagues at the London School of Hygiene and Tropical Medicine.

Q Who is paying for the study?

A Since 1990 the study has been funded by the Department of Health and the Scottish Executive Health Department. Funding presently runs until June 2005 and we are currently applying for further funding.

Q Have the control groups recruited for this study changed since the start of the study in 1990?

A Yes. Controls are recruited to be representatives of the general population who do not have CJD and there are different ways of recruiting controls, each with its own pros and cons. Up until a few years ago we were recruiting two groups of controls- hospital controls (people in hospital with a non-CJD illness) and GP controls (people registered with the same general practice as the person with CJD). In 2002 we stopped recruiting GP controls because of problems (see below) and changed to ‘relative-nominated controls’ and general population controls. We asked the National Centre for Social Research to recruit this last group as a once off activity.

Q Which control groups are recruited currently?

A Hospital controls (see above) and relative-nominated controls. To recruit relative-nominated controls our research nurses ask relatives of those with CJD to ask a friend of theirs to take part in the study. Ideally this friend should have a relative (the control) who is roughly the same age and gender as the person with CJD. The nominated friend is then contacted by one of the research nurses. If the friend agrees, the research nurse will ask the friend’s relative (the control) if they will take part in the study. If both the friend and their relative consent to take part, the research nurse will interview the friend about their relative using the same risk factor questionnaire as is used for people with CJD.

Q Will I be asked to take part in nominating a relative-nominated control?

A Quite possibly. If you have a close relative who has recently been diagnosed with CJD, you may be asked to nominate a friend when the team from the National CJD Surveillance Unit first visit your relative. However, if you are a relative of someone who was diagnosed some time ago (before 2001/2), we will not be asking you to take part in this section of the study.

Q Who will I meet if I agree to take part in the study?

A We have two trained research nurses. One of them will talk to you about the study and, if you agree to take part, they will interview you about your relative with CJD. Their names are Mrs Blaire Smith-Bathgate (b.smith-bathgate@ed.ac.uk) and Ms Margaret Leitch (margaret.leitch@ed.ac.uk). Sometimes, if both of the research nurses are busy elsewhere, one of two neurology specialist registrars will speak to you and interview you about the study; they are Dr Craig Heath (craig.heath@ed.ac.uk) and Dr Katy Murray (katy.murray@ed.ac.uk).

Q What are the difficulties in carrying out a case control study?

A The main problem we have faced in the past has been getting people to agree to be controls. This is why we have opted for 'relative-nominated controls', in that hope that your friends will be more willing to participate and contribute to the study than strangers. A second potential problem is what is known as 'recall bias'. This occurs when the information we receive about people with CJD is influenced by what the relative being interviewed thinks about CJD. This may occur when the relative has read and spoken to people about CJD. That is why our research nurses ask to interview you about your relative as soon as possible, normally at the initial hospital visit.

Q Have there been these problems with this study

A Yes and no. The vast majority of relatives have been extremely generous and have agreed to be interviewed about their relative with CJD by one of our research nurses at the initial visit from the National CJD Surveillance Unit, which is organised in collaboration with the National Prion Clinic, London. In addition, since we have been recruiting relative-nominated controls, many relatives have also kindly asked a friend to help by taking part in this study as part of the control group. However in the past, we did have a poor response rate recruiting controls from the same general practices as those with CJD, hence the change to recruiting relative-nominated controls. These are now the main control group.

Q Why choose a case control study and not another type of study?

A Case control studies are one type of study used by scientists called epidemiologists to study why, where and when diseases happen so that they can prevent diseases in the future. Case control studies are useful in studying relatively rare diseases like CJD where there are many possible risk factors. There are other study types which are better for investigating more common diseases, for example high blood pressure, where groups of people are followed over time to see if they get the disease (cohort studies) or for investigating possible interventions, for example new treatments (randomised controlled trials).

Q I am a relative of someone with CJD. How can I help with the case control study?

A Thank you! There are three main ways you can help. First by agreeing to be interviewed by one of our research nurses about possible risk factors your relative with CJD may have been exposed to. This is usually done at the time of the initial hospital visit by the team from the National CJD

Surveillance Unit. Second, you could ask a friend to take part in the study as part of the 'relative nominated control' group. The research nurse will ask you at the initial visit if you have a friend who would agree to be interviewed about a relative of theirs (the control). Ideally the relative of the friend would be roughly the same age and gender as your relative with CJD, but this is not absolutely necessary. Last, if you have already taken part in the study, you can help others to make the same decision by telling them what it involves.

Q What results have been found so far?

A We are in the process of analysing the data and hope to submit a paper for publication early in 2005.

Q How can I find out more information?

A You can contact Mrs Blaire Smith-Bathgate in the first instance (0131 537 3089 or b.smith-bathgate@ed.ac.uk) or Ms Margaret Leitch (0131 537 2083 or margaret.leitch@ed.ac.uk) or myself, Dr Hester Ward (0131 537 3091 or h.ward@ed.ac.uk). Any of us will be happy to answer any questions you may have about this study.

I would like to thank all the families who have taken part in the study so far. Without their on-going support and collaboration we would not be able to carry out this research. I would also like to thank Simon Cousens for his help in the preparation of this article.

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Research strategy of the Department of Health and the problem with prions

Dr John Stephenson, Senior Research Officer at the Department of Health, gave an excellent talk at the Network's 'Meet the Expert' family support meeting on Saturday 13 November. This is a selection of his slides.

This is the first of a series of lecture articles where experts give information at a glance with a 'bullet-point guide' to prion disease

What is so different about Transmissible Spongiform Encephalopathies (TSEs) ?

- They can be transmitted between individuals, but are genetically determined
- They do not contain a nucleic acid, eg DNA
- They do not produce an immune response
- The transmissible agent (prion) is a human protein
- The transmissible agent does not differ from the host protein in sequence, but in its three dimensional structure

How do prions work?

- We are unclear how prions work, but normal prion alters its shape, which in turn catalyses other normal prion to do likewise. How exactly the abnormal prion causes cell damage remains unclear

The origins of vCJD

- Meat contaminated by neural tissue
- Consuming infected offal
- Vaccines
- Cosmetics
- Baby food
- Pet food
- 'Institutional' food using mechanically recovered meat
- The exposure probably took place many years ago with the greatest risk occurring in the 1980s and early 1990s

Why are TSEs such a problem for the NHS ?

- There is no cure, the disease is 100% fatal
- There is no vaccine
- There is no diagnostic test – no unique gene, protein or immune response
- Potentially all the UK population could have been exposed and could be carriers.
- Prions adhere to surgical steels and are resistant to standard decontamination protocols

The Department of Health research strategy

- How widespread is the problem?
- Can we diagnose the disease before clinical symptoms?
- Can we protect blood transfusions and organ and tissue transplants?
- Can we find a cure?
- Can we thoroughly clean surgical instruments?

Epidemiology (study of the disease in the population)

- Surveillance by the NCJDSU in the UK and throughout Europe
- Mathematical modelling
- Special attention to high risk groups – eg haemophiliacs
- Case control study
- Retrospective and prospective surveys of the young and elderly
- National tonsil archive

Organ and tissue transplantation – what tissues are infectious?

- Brain
- Spinal cord
- Tonsil
- Spleen
- Possibly other lymphoid tissues including the gut
- Others appear to be negative but we cannot be sure until the research is complete

Protecting the blood supply from CJD

Future desirable developments to allow this would include:

- Preparing the blood service for a screening test
- A direct blood test to screen patient blood
- A direct blood test to identify potential infected donors
- Treatment of donor blood to remove infection

Difficulties of TSE drug development

- The normal protein is present in many tissues of the body
- The function of the protein is unknown.
- The 'rogue' protein differs only in its shape
- Drugs which would alter the shape of the prion could alter the shape of many other proteins, which would cause side effects
- Drugs need to get into the brain.
- As CJD is a very rare disease, little commercial interest in developing drugs.

Challenges in setting up clinical trials for human TSEs

- How do you design convincing trials involving small numbers of patients?
- Should patients be entered into trials with potentially toxic drugs?
- Should patients be entered into trials of drugs based on cell culture data alone?
- Should very ill patients be moved large distances for research purposes?
- As these diseases are invariably fatal does this justify trying any potential cure?
- Should you treat 'at risk' people, eg close relatives of those with the inherited forms of disease or recipients of potentially infected blood donations?

Decontamination of surgical instruments

Development of a test to screen potential infected surgical instruments

- Rapid and easy screening of instruments after processing
- Capable of detecting very low levels on surfaces and even in crevices and cavities
- Screening test should be easy to use. ie Capable of detection by eye, or under UV light

Decontamination research already underway includes:

- A co-ordinated programme overseen by a steering group
- Studies on stainless steel surface chemistry
- Studies on ultra-sensitive detection systems
- Testing of 'prion' detergents and solvents
- Testing of 'prion' enzymes to 'wash off' infection
- Consideration of other methods such as plasmas, high-energy beams and rocket fuel

Decontamination progress to date

- Several ways to develop low levels of prions have been detected
- Several decontamination technologies have shown to be successful in the laboratory
- Several decontamination technologies are expected to come to market in 2005
- A Science and Engineering Group is being set up to facilitate the introduction of new technologies into the NHS

Proposed prion therapeutic agents (alphabetical order)

- Antibodies and vaccines
- Blockers of prion aggregation
- Chlorpromazine
- Dextran and similar substituted sugars
- Diazo dyes
- NSAIDs – including aspirin
- Pentosan polysulphate
- Protein 'chain busters'!
- Quinacrine

The PRION-1 clinical trial of an anti-prion drug

Articles adapted from the national Prion Clinic PRION-1 newsletter

The PRION-1 study is now up and running. It is a collaboration between the NHS National Prion Clinic (NPC), and the Medical Research Council's (MRC) Prion and Clinical Trial Units to bring together the specialist expertise required for the careful testing of anti-prion drugs that may be suitable for study. Quinacrine is the drug that is currently being tested, however the study has been purposely designed as a framework to test not only quinacrine, but also other potential drugs as they become available.

The National Prion Clinic is the national specialist NHS clinic for patients with CJD and other forms of prion disease. The MRC Prion Unit is a centre of excellence for research into understanding prion diseases and developing new treatments. The MRC Clinical Trials Unit specialises in designing studies for testing treatments to see if they offer a real benefit to patients in a scientifically rigorous and ethically acceptable way.

Testing an anti-prion drug will be difficult. The diseases affect different patients in different ways and progress at different speeds irrespective of the effect of any drug, and some patients will already have substantial irreversible brain damage by the time diagnosis is made. To get a clear answer whether a new drug is having a worthwhile effect is likely to require studying quite a

large number of patients over 2-3 years. As prion diseases are rare, this means that for the study to succeed, most patients in the UK affected by prion disease would need to participate. We have worked hard to try to develop a study that is available and acceptable to the majority of patients. An in-depth consultation with patients, families and carers was carried out by the MAC to inform the study design. In order to make the study available to all patients, a National Referral system has been introduced whereby all neurologists in the UK have been asked (subject to their patient's consent) to refer all patients not only to the National CJD Surveillance Unit in Edinburgh (NCJDSU), but also to the NPC, so everyone has the opportunity to find out about treatment options and other studies available.

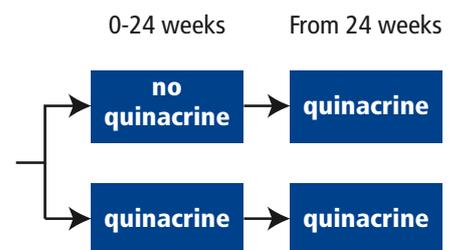
It is important to be realistic about any early potential treatments for CJD. Quinacrine may not be a 'cure' but may well have significant benefit for some patients and in evaluating this possible benefit we will learn much more, not least a great deal about the best way to evaluate treatments for a group of diseases that vary so much in their course and duration. This knowledge will in turn allow us to design better studies for future treatments which we hope will emerge in the years ahead from ongoing research in the MAC Unit and elsewhere.

What is involved?

The PRION-1 study, which is the first generation of studies to evaluate treatments for prion disease, has three different parts and participants are free to choose which, if any, part they would like to join. This is discussed in detail during the consent process.

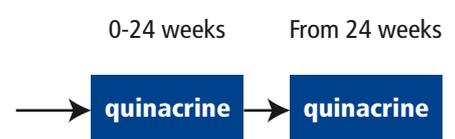
A: Randomised study

Scientifically speaking, the best way to find out if quinacrine offers overall benefit, is by what is called a randomised controlled study. What this means in this study is that people are divided randomly into two groups, one group receiving quinacrine immediately and the other receiving quinacrine six months (24 weeks) later. Neither patient nor their doctor would choose which of these groups was allocated but they will know whether or not they are taking quinacrine because no placebos (inactive dummy pills) will be used.



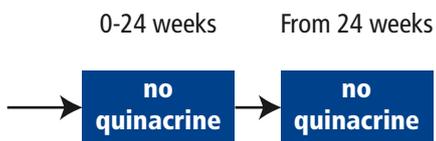
B: Non-randomised study

We understand that some people may prefer not to be randomised, as they don't want to wait to take quinacrine once they have decided on this course of action. We therefore offer the option to start the treatment straight away.



C: 'Natural history' non-randomised study

We also understand that some people may choose not to take quinacrine but would still want to contribute to research to understand these diseases better, which will help us with assessing treatments in the future. These people can enter a 'natural history' study in which we carefully monitor the disease.



It is preferable if patients come to the National Hospital for Neurology in London for the study visits and we have a dedicated ambulance specifically for this purpose to ensure a minimum of disruption. However we understand that this may not always be possible, and study staff can also visit patients at home to carry out assessments if necessary.

Assessments

Firstly, a 'baseline' assessment is carried out. This is a detailed evaluation for everyone at the start of the study. If the patient chooses to take quinacrine, then there are some additional tests to make sure that quinacrine is safe for that individual. The clinic staff spend whatever time is needed to answer questions about the study. We agree with patients and their families a plan of subsequent follow up visits and monitoring for any side effects of quinacrine. Visits may be as frequently as monthly to begin with, but then are more likely to be every two to three months or in some patients less frequently. The staff are always contactable and happy to discuss any issues at any time between visits.

Neurological examination

A detailed neurological examination is carried out at each visit. This is carried out in a very standardised way and recorded by digital video. We all want to see our patients

getting better, and it is easy to mistakenly think that this is happening. For this reason we have an independent neurologist with no previous knowledge of the person concerned review the digital videos to provide a separate assessment in a way that will not be biased by previous contact with the patient and their family. This is extremely important to allow us to evaluate change in what are complex progressive neurological diseases.

Blood tests

Blood is taken at each visit for a number of reasons: to continue to monitor the safety of quinacrine; to study markers that may be helpful in detecting response to treatment; and to store a sample so that we can get the benefit of applying new tests as they become available. We are also actively working on research to develop new diagnostic tests. Such tests will be very important in the future in order to prevent people becoming infected via, for example, blood transfusions. Blood samples therefore, are a vital contribution to progressing research in these diseases.

Interviews with trial participant and their family and/or carer

These are important at each assessment point so that our observations and assessments are put in the context of reports by the person with prion disease and those who see them every day. It is common for the condition to fluctuate, with good days and bad days and from week to week.

Other tests

There are other important tests that can provide valuable information. These include MRI brain scans, EEG (a recording of brain waves), and spinal fluid testing, all of which are likely to have been carried out at least once already in diagnosing this condition, but which may also help us follow the course of the disease. Some of these may be repeated at regular points in the study, if appropriate, and with the agreement of the participant. These tests will be elaborated further in the next PRION-1 newsletter.

All information collected during PRION-1 will be confidential.

Secondary transmission causes concern

The Health Minister, John Reid, announced in December 2003 that a patient had died of CJD and it was thought, although not proven, that this was the first case of CJD where transmission had been as a result of a blood transfusion.

In August 2004 it was announced that a second patient had died after a blood transfusion from a donor who had subsequently died of vCJD. The second patient had died of an unrelated cause but a post mortem showed that prion was present in the spleen and cervical lymph nodes. As all the patients to have died of vCJD had been from the methionine homozygous PRNP genotype (mm) this case showed that vCJD is not confined to this group as the patient was a heterozygote at codon 129 of PRNP (mv). According to Peden et al these findings have major implications for future estimates and surveillance of vCJD in the UK. [www.thelancet.com Vol.364 August 7, 2004]

In September 2004 John Reid announced that selected groups of patients were being notified that, as they had received certain batches of plasma products in the past, they could be at a small increased risk of carrying the vCJD agent. The people who were affected (around 6,000) were from the haemophilia fraternity and other bleeding disorders. The Haemophilia Society has issued an excellent fact sheet for their members and this can be viewed at www.haemophilia.org.uk.

CJD Support Network Management Committee 2004-05



Dr Angus Kennedy
– Chairman
Consultant Neurologist



Michael Bradley
Michael's mother died of Sporadic CJD



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



Jean Lightband
Jean is a neurological specialist nurse at the National Hospital for Neurology and Neurosurgery



Mike Curtis – Treasurer
Mike a former bank employee is currently nursing his wife with Sporadic CJD



Roger Tomkins
Roger's daughter Clare, died of vCJD



John Gilbert – Assistant Treasurer
John's brother in law died of Sporadic CJD



Sarah Tomkins
Sarah's husband Edward died of Sporadic CJD



John Williams
John is a retired Government engineer whose daughter, Alison, died of vCJD



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



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

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



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



Gillian Turner
CJD Support Network co-ordinator

Who's who in CJD

National Prion Unit



Professor John Collinge CBE
Professor of Neurology and Head of Department of Neurodegenerative disease, Director of MRC Prion Unit



Dr Stephen Wroe
Consultant Neurologist, Clinical Trials co-ordinator. National Prion Unit

National CJD Surveillance Unit



Dr Richard Knight
Consultant Neurologist, Director of the National CJD Surveillance Unit



Professor James Ironside
Consultant Neuropathologist, National CJD Surveillance Unit



Professor Bob Will
Consultant Neurologist, National CJD Surveillance Unit

CJD Support Network membership application

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

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

There is no fixed subscription, but you may wish to make a small donation to cover the cost of production and postage of our newsletter.

- £8 £12 £25 £50 Other

Please make cheques payable to **CJD Support Network**

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

Name Title

Address

Postcode

Telephone Email

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

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

I want all my donations to the CJD Support Network from 6-April 2000 to be Gift Aid until I notify you otherwise.

Use Gift Aid and you can make your donation worth more. For every pound you give to us, we get an extra 28 pence from the Inland Revenue. To qualify for Gift Aid, what you pay in UK income tax, capital gains tax or tax on interest from savings must at least equal the amount we will claim in the tax year. Please let us know if you move or if you no longer pay enough tax to cover the money we claim back from the Inland Revenue.

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The views expressed in this Newsletter are personal and not necessarily those of the CJD Support Network.

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