

Government response to CJD

Gordon McLean, National CJD Surveillance Unit

In October 2000, in response to the conclusions of the BSE Inquiry, the government put in place a sum of money to be used to help improve the care provided for people affected by vCJD. The hope was also to be able to give a more timely response to the needs of people affected by vCJD.

With the expectation that this fund was to be accessed via the National CJD Surveillance Unit, we put forward the recommendation that it was not only those affected by vCJD who should benefit from the care package but those with any form of CJD and prion disease. The government, the CJD Support Network and the Human BSE Foundation, which fought hard for the care package, all agreed, and £1million was put in place to help with the care of those affected by these rapidly debilitating fatal diseases.

The care package will work in conjunction with local health and social services. It will not be the sole source of funding for the care of someone with CJD, but is available to cover any shortfalls in local authority care provision. Essentially the package is available for those families who wish to care for the person affected by CJD at home with adequate assistance. Unfortunately some difficulties accessing services may still remain owing to lack of local resources.

The care package can be accessed to assist with the provision of all health and social care needs. This may include needs such as extra nursing care, physiotherapy, adaptations to the home, quicker access to equipment, accessing aromatherapy, respite care,

counselling and anything else which has been assessed to be essential to meet the patient's and their family's individual needs.

Although the care package is accessed through the Surveillance Unit via the national care co-ordinators, the co-ordinators do not have direct access to the fund. To access the care package, an invoice needs to be raised by the finance department of the local health authority and this will be for both social and health needs. For example, if social services have provided a service to a patient for which they would like reimbursement from the care package, provided this has been deemed acceptable by the co-ordinators, a health authority invoice for the agreed amount should then be forwarded to the co-ordinators to be processed. Funds will then be forwarded to the health authority, which will then send appropriate funds to social services.

The main emphasis is on trying to establish a triumvirate of funding between health, social services and the CJD care package. This requires open communication between the three partners and the ability to respond as quickly as required to the patient's and their family's needs, attempting to cut down the barriers that sometimes occur when implementing health and social care.

A CJD advice network was also established. The network comprises a variety of professionals – district nurses, occupational therapists, physiotherapists, general practitioners, clinical nurse specialists, counsellors, social workers, dentists, charity representatives and others – all of whom have had direct involvement with CJD and those affected by it.

The advice network aims to enable professionals who are presently caring for someone with CJD to be able to make direct contact with an individual from the same profession for advice and to share information about experiences. This sharing of information will help to ensure that a high quality of care is established for all people affected by CJD.

We hope that having all these actions in place will help relieve some of the burden that is placed on families' and professional carers' shoulders when caring for someone with this fatal and debilitating disease.

Editor's note: The CJD Support Network acknowledges the unstinting work of the Human BSE Foundation and its solicitor, David Body, which helped to achieve this response from the Department of Health.

ON OTHER PAGES

- 2 News
- 4 Treatment and prophylaxis for CJD
- 6 Treatment for CJD
- 7 Quinacrine trials begin
- 8 The National Prion Clinic
- 9 Fundraising
- 10 Letters
- 12 CJD research views
- 13 vCJD and blood
- 14 Dental treatment preferences
- 15 CJD Support Network

CJD Support Network AGM

The annual general meeting was held on Saturday 6 October 2001 at the Hilton Hotel, Leicester. The meeting was felt by those who attended to be the best to date. Sixty members attended and listened to an excellent presentation by Dr Philip Monk, director of public health in Leicester, and his colleague, Dr Gerry Bryant, on the report on the vCJD cluster at Queniborough, Leicestershire. The meeting heard about their thorough research on the issues surrounding the cluster.

A summary of their research was featured in our last newsletter and the full text of the report is available through the Leicestershire health authority website <http://www.leics.ha.org.uk>

In contrast, Professor John Collinge gave an in-depth view of CJD, the work of the Prion Unit and the research and drug trials being undertaken. Details can be seen in Kathryn Prout's article on the Prion Unit at St Mary's Hospital, page 8.

Network chairman receives MBE

Clive Evers, former chairman of the CJD Support Network, was awarded the MBE by HRH Queen Elizabeth II for his work with the Network. He attended Buckingham Palace on 30 October 2001 to receive his award.

Gillian Turner and all the members of the CJDSN would like to congratulate Clive.

The Prince of Wales Awards

The Network would like to congratulate Kathryn Prout, clinical nurse specialist at the Prion Unit at St Mary's Hospital London and also a co-opted member of the management committee of the Network, on being named a 2001 finalist at the Prince of Wales Awards for Health Care in London.

Kathryn's guest at the ceremony at St James's Palace on 16 July was Maria Bryne. Maria is also a member of the Network's management committee and lost her husband Graham through GSS.

House of Lords

Clive Evers, Bill Mitchell and Gillian Turner were guests of the Life Neurological Research Trust at a fundraising dinner in memory of Baroness Wharton, held at the House of Lords on 5 October 2001.

Baroness Wharton died from classical CJD and her family started the Life Neurological Research Trust to raise money in her memory to further research into all neurological conditions. In the trust's first year all the money they raise is to be given to the CJD

Support Network/Alzheimer's Society to fund research into the cause, cure and care of CJD.

The CJD Support Network in Japan

Gillian Turner of the CJD Support Network was in Japan when families won their case in court on Wednesday 14 November 2001. The Tokyo district court found the state and two pharmaceutical companies (B Braun Melsungen AG, a German medical equipment manufacturer, and Japanese importer Nibon B SS) responsible for the spread of brain-wasting CJD in Japan and urged them and the plaintiffs to reach a settlement as early as possible to resolve the case. The case involved 28 victims (25 of whom have already died).

The court found that the two firms could have foreseen as early as December 1978 that dura mater, the fibrous membrane surrounding the brain and spinal cord often used in transplants, could transmit the disease but failed to take sufficient measures to ensure the safety of their products. The court also said that the state bears responsibility as it failed to take effective measures to prevent the spread of CJD in Japan by banning the use of allegedly CJD infected dura mater after the first case of the disease was reported in the US in February 1987.

Another court case in Otsu district court, Japan, is expected to repeat the findings for further cases.

The CJDSN is now helping colleagues in Japan to set up a carers support network.

The Daily Yomiuri – Kansai/National. Friday 16 November 2001

Dates for your diary

International CJD Day
12 November 2002

Memorial service
17 November 2002
Details will be given in a future newsletter

CJD Figures

Figures released on 6 September 2001 from the National CJD Surveillance Unit showed that there had been a 30 per cent increase in cases of variant CJD in the previous year. Professor James Ironside warned that many people could already be infected, but would not have any symptoms yet. Professor Ironside also stated that Northerners and people living in Scotland were more likely to have contracted the disease, which is probably due to dietary factors in the 1980s.

The more recent figures below show the number of suspect cases referred to the CJD Surveillance Unit in Edinburgh, and the number of deaths of definite and probable cases in the UK up to 7 January 2002.

Summary of vCJD cases

- Number of definite and probable cases of vCJD (deaths) as above: 104
- Number of definite and probable cases of vCJD (alive): 9
- Total number of definite and probable vCJD (dead and alive): 113

CJD Support Network new publications

The following new factsheets are now available from the CJD SN office (see back page):

- Aggressive behaviour in CJD
- Swallowing problems
- The autopsy in patients with suspected CJD

REFERRALS OF SUSPECT CJD		DEATHS OF DEFINITE AND PROBABLE CJD						
Year	Referrals	Year	Sporadic	Iatrogenic	Familial	GSS	vCJD	Total Deaths
1990	[53]	1990	28	5	0	0	-	33
1991	75	1991	32	1	3	0	-	36
1992	96	1992	44	2	5	1	-	52
1993	78	1993	37	4	3	2	-	46
1994	116	1994	51	1	4	3	-	59
1995	87	1995	35	4	2	3	3	47
1996	134	1996	40	4	2	4	10	60
1997	161	1997	59	6	4	1	10	80
1998	154	1998	63	3	4	1	18	89
1999	169	1999	61	6	2	0	15	84
2000	178	2000	48	1	2	1	28	80
2001*	170	2001*	37	3	2	2	20	64
Total Referrals	1471	Total Deaths	535	40	33	18	104	730

*As at 7 January 2002

Treatment and prophylaxis for CJD

Dr Stephen Dealler, Consultant Medical Microbiologist, Burnley General Hospital



One of the first things that we should stop saying to our patients is 'There is no treatment for CJD and none is thought possible'. Opinions that were held in the past – that there are no answers – are now being revised.

The article in the Mail on Sunday on 12 August suggesting that Rachel Forber, a 20-year-old woman from Warrington, had been cured by the use of quinacrine may have been misleading. However, Rachel was deteriorating rapidly before the drug was started.

The major problem with CJD is that symptoms are the result of the damage that has taken place in the brain caused by the disease process. Initially, brain cells are inhibited from working

properly by the chemistry of the brain reacting to the irritation of the disease. It is at this point that symptoms start to appear. After a relatively short period some of the cells die and the damage becomes irreversible. This cell death takes place through a process called apoptosis; cellular suicide occurs as a result of toxic damage.

Already we can see that there may be a chance that the prions growing in the peripheral tissues and the brain could be stopped and the destruction of the brain prevented. I will try to explain the action of the drugs that are currently being considered after animal and test tube experiments.

[Editor's note: Rachel has since died of vCJD. See page 7.]

Pentosan polysulphate

(see <http://www.airtime.co.uk/bse/pentrev.htm>)

Pentosan polysulphate was first used to stop the growth of certain viruses. More recently it has been shown to do the same for some bacteria. As a result, in the early 1980s, pentosan was injected into mice and hamsters which had been injected with scrapie at around the same time. Not only did the drug stop the disease from taking hold, one dose actually removed all the disease present from the animal's body. Later, pentosan was shown to be extremely powerful in its ability to stop the growth of prions in test tube cell cultures, removing all prions from the growing cells.

One might infer from the way in which pentosan polysulphate interacts with prion molecules that it might also work on all forms of CJD. However, the drug cannot penetrate a rodent's brain (nor that of any other animals) Therefore, once the scrapie has entered the central nervous system, the drug is useless.

In humans pentosan has been used for many years as an anti-coagulant. When given orally it has almost no side-effects and can be used as a treatment for an inflammatory condition of the bladder. It was therefore quickly realised that the drug might be used as a prophylactic against CJD. If, for example, someone had been injected with infected tissue in a laboratory, pentosan could be given to that person and we might expect it to prevent disease from taking place. The problem has been that no experiments could be carried out to demonstrate its efficacy in humans. As a result pentosan polysulphate has not been given a licence in the UK; anyone needing it must have it specifically prescribed by a doctor.

Dapsone

(see <http://www.airtime.co.uk/bse/dapsone.html>)

A researcher in the USA¹ decided that the progressive damage that took place in the brain in CJD was caused by the chemicals around the cells that were dying. She believed

that local inflammatory stimulants might be stopped through using aspirin-like compounds and dapsone, a drug used for the last 40 years to treat leprosy.

When the researcher gave the drug to mice incubating CJD, she found that the incubation period was much longer than normal. She put this down to the drug preventing the prions clumping into plaques (as had been shown in Alzheimer's disease) and the neurotoxicity of the plaques themselves.

Dapsone has low levels of side-effects and is easily available but it may have to be given to patients before they have symptoms. One patient with symptoms has been said to have improved with the drug. However, this must not be assumed until full diagnostic trials are carried out.

Quinacrine

(see <http://www.airtime.co.uk/bse/quinacrine.html>)

Quinacrine is an anti-malarial that was used before the second war. It was found to be effective against

gut parasites and then, later, against uncommon skin conditions. Much better anti-malarials and anti-parasitic reagents are now available but, because of its dermatological use, the drug remains available. In 2000, quinacrine was found to be effective in preventing the multiplication of prions in cell cultures² and, unlike pentosan polysulphate, it was thought to penetrate the central nervous system. After the work was repeated³, it was therefore given to symptomatic patients with CJD.

Quinacrine is a fluorescent dye that interacts with many proteins and DNA but its mode of action is still not known. Claims by Rachel Forber's father that she had not greatly deteriorated after the drug was started and that her higher brain functions had improved were exciting. However, we must await larger scientific studies currently being organised through Professor Collinge at Imperial College London. Quinacrine has few side-effects when given in standard doses. However, Rachel received three times the standard dose (and had side-effects) in order to keep high levels in the brain. Without proof that it works, the drug could only therefore be given in lower doses if used as a prophylactic.

Flupertine

(see <http://www.airtime.co.uk/bse/flupertine.html>)

Flupertine is an analgesic that acts inside the brain to decrease pain all over the body. Unlike morphine, which acts in a similar way, it is not addictive and has no effect on the gut. However, flupertine has not been used much outside Germany because it is not very powerful.

Flupertine's mode of action seems to involve changing the levels of glutathione inside cells, and it was realised that it would stop the apoptosis of brain cells seen in CJD. The drug was given to 23 patients with CJD. The patients have appeared to improve, presumably because the drug permits the cells to continue action.

In Germany flupertine has been used by general practitioners and has been widely prescribed. However, it is not available as a licensed drug in the UK and as such it must be prescribed by a doctor for an individual patient.

Multiple drugs

It seems clear that the methods by which dapsone, quinacrine and flupertine work are all different. The structure of pentosan polysulphate, which is a long highly charged molecule unlike the others, probably means that it acts in a different manner as well. Because of this, and because of the low rate of side-effects seen as a result of the drugs, it would be reasonable to consider the use of several of them together: for example, dapsone with quinacrine and flupertine for a patient with symptoms. For someone late in the incubation period but without symptoms it may be reasonable to use just dapsone and low dose quinacrine. For someone who has recently been inoculated with disease, it may be best to use pentosan polysulphate by itself. Trials with multiple drugs have not been carried out in animals, however.

Are these drugs worth trying?

A diagnostic test to establish whether the level of infection in someone's body is changed by these drugs is still awaited. Potential tests may be available soon but until then we cannot be certain as to whether the drugs will work. Simply showing that they act in animals and in test tubes does not bring certainty that they will work in humans. However, the modes of action indicated by other research into pentosan polysulphate, flupertine and dapsone suggest that they would be expected to have some action on the human forms of the diseases. This uncertainty and the severity of the disease must be balanced against the pharmaceutical side-effects when deciding whether or not individuals

should consider taking the drugs for long periods.

CJD has always had the problem that, without a diagnostic test, we are having to treat only patients with symptoms. Brain damage has already taken place and so major improvement may not be possible. However, the possibility of using these drugs in patients who may be incubating the disease must always be considered in familial forms of CJD or GSS. In these people, the genetic change can be found and the chance that they will develop disease calculated. If the patient considers this risk to be too high and is willing to try multiple drug therapy then the treatment might be considered by the doctor.

Around the corner

The diagnostic tests on the way may allow us to see if drugs work in humans; drugs that are more toxic (see <http://www.airtime.co.uk/bse/treatmentall.html>) may be considered. Diagnostic tests may also mean that larger numbers of asymptomatic people are diagnosed, having given blood for transfusion or been in hospital for some other reason. A larger market for treatments would mean that the drug companies may be keener to provide better answers.

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Treatment for CJD

Dr Richard Knight, Consultant Neurologist, National CJD Surveillance Unit



Any news of possible treatments for an illness, particularly one which is inevitably progressive and fatal, must be very welcome to anyone involved with the disease. However, one needs to greet such news with a degree of caution. It is wonderful to have hope, but individuals can feel cruelly let down when hope is not fully realised. A clinician has a duty to give new information in a balanced way: to inform patients and families of advances in knowledge and possible treatment developments, while explaining the inevitable potential difficulties and uncertainties.

The potential for drugs

Over the last few years there has been increasing understanding of the disease processes which occur in the brains of individuals with CJD. Understanding these biological and chemical processes may suggest drugs which could, in theory, slow or stop the development of illness. However, it is important to realise that medicines which could or should work in theory are not always useful in practice. A number of 'designer drugs' for various conditions have proved disappointing in practical use. On the other hand, some very useful treatments are discovered entirely by accident and the way in which they work understood only later. This is not to deny the importance of fundamental scientific knowledge; it is simply to emphasise that such knowledge does not always lead straightforwardly to useful treatment. Also, the lack of fundamental knowledge does not always prevent the development of treatment.

Testing of drugs

In the design of treatments for CJD, potential drugs may be tested 'in vitro' by using chemical or isolated cell systems. Through such experiments a number of drugs are known to have a marked effect on the basic CJD processes. However, these cannot be a substitute for seeing the effect of drugs in animals or humans. Testing may be undertaken in animal models of prion illnesses, but, again, these cannot be complete substitutes for seeing how treatments affect human beings with CJD.

Fundamental treatment

When drugs are used, it is important to differentiate between symptomatic effects and fundamental effects. Symptomatic effects are effects on symptoms of the disease but not on the actual disease process. Fundamental effects are those in which the drug specifically slows, arrests or reverses the disease process itself. This is not to say that symptomatic effects are not important. Clearly, if one gives an individual with a disease a drug which improves them in some way, it must be a good thing. However, in a progressive, fatal

disease such as CJD one would really wish for treatment which has fundamental effects. As a specific example, there are reasons for thinking that quinacrine could have some symptomatic effects in individuals with CJD, without necessarily affecting the underlying progression of disease.

CJD causes damage to and death of brain cells. It is therefore very important that any fundamental treatment is given as early as possible. At present, diagnostic tests exist which are inevitably positive at a stage when there has already been neurological damage. The development of successful treatments for CJD should therefore go hand in hand with the search for earlier and more accurate diagnostic tests.

Therapeutic requirements

In the treatment of CJD, there are two broad considerations. First, there is treatment of those individuals in whom a diagnosis of CJD has been made. It might well be that individuals affected by the disease, their families and their clinicians would be prepared to try treatments which are difficult to administer and have potential for serious side-effects. It might be argued that if an individual has an inevitably progressive and fatal condition, one might be prepared to run certain risks in the hope of benefit.

The second therapeutic situation is one in which an individual might go on to develop CJD (for example, because of an inherited abnormal gene or some previous exposure to infection). These individuals will be currently healthy and, depending on individual circumstances, may not develop CJD at all. In such circumstances, it would be extremely important to ensure that any therapy is safe to take over potentially long periods of time.

Conclusion

It is promising that there are a number of possible treatments being considered for CJD. However, the real test of any treatment is how it works in individuals with disease. It is therefore vital that any theoretical claims or suggestions from individual cases be properly investigated in careful clinical trials. Given the nature of CJD, it should be relatively easy to determine whether any specific treatment has a significant useful effect in delaying, halting or reversing disease progression.

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Trial of treatment for Creutzfeldt-Jakob disease announced

In this article, taken from a Department of Health press release, CJD refers to all types of CJD, ie sporadic, familial, iatrogenic and vCJD

The Department of Health has asked the Medical Research Council (MRC) to fast-track the design of a clinical trial to evaluate the effectiveness of quinacrine (Mepacrine) as a potential treatment for Creutzfeldt-Jakob disease (CJD). Further information on plans for a UK trial will be made available as soon as the research details have been finalised. In the meantime, information from patients already in treatment is being gathered.

The initiative follows the treatment of a woman from Britain with vCJD in San Francisco. This was based on a publication of preliminary laboratory evidence by Dr Prusiner's research group in San Francisco¹. The publication shows that quinacrine, and to a lesser extent chlorpromazine, inhibit the formation of a disease-associated form of the prion protein in mouse brain cells grown in the laboratory.

Chief medical officer, Professor Liam Donaldson, said:

'The research in the USA involving quinacrine has suggested that it may have some benefit for people with CJD. This has raised the hopes and expectations of such patients and their families. I have asked the Medical Research Council to design a trial that will evaluate the efficacy and potential side-effects of the drug quinacrine so that we have this information as soon as possible.'

'This drug has been used for many years as an anti-malarial agent, but it is not licensed for use in the treatment of human prion diseases. The decision to evaluate quinacrine does not mean that we regard it as a 'front runner' in finding an effective treatment for CJD. Simply it means that any credible research claim which might offer hope in an otherwise fatal disease must be evaluated. Other avenues of research to produce an effective treatment are underway, notably work being undertaken by the MRC Prion Unit at Imperial College.'

Further work is essential in order to establish whether this drug can provide an effective treatment. Proper assessment needs to be carried out in a well-designed clinical trial. The trial will aim to determine whether quinacrine has any beneficial effects for people with CJD and, in the usual way, a trial steering committee will be established to oversee the trial in line with MRC guidelines for good clinical practice.

Those involved will be the National Prion Clinic², the MRC, through its Prion Unit³ and Clinical Trials Unit⁴, the National CJD Surveillance Unit (NCJDSU)⁵ and the Department of Health. Neurologists will be informed separately of the details of the trial. Patients and relatives of patients who currently have CJD will receive further information about this treatment and the option of joining the clinical trial from their clinicians. It remains essential to the surveillance of CJD and to the success of clinical studies that the NCJDSU continues to be informed of all new potential CJD cases.

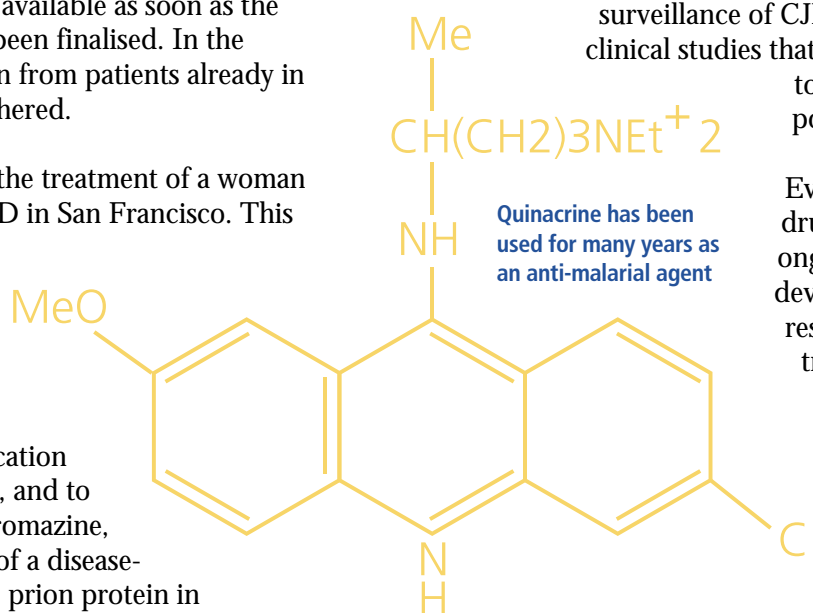
Evaluation of this particular drug is only part of an ongoing programme of drug development by UK researchers for potential treatments for CJD. A number of compounds for new candidate therapies are currently being studied and in the near future will need to be assessed for their suitability for clinical

trials. A new advisory committee will be set up by the chief medical officer to report to the Department of Health on this.

Editor's note: Sadly, since this announcement was made, the woman being treated by Professor Pruisner died (Mail on Saturday, 1 December 2001). See page 4. We would like to send our sincere condolences to her family.

References

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- 2: Professor John Collinge, National Prion Clinic, Department of Neurology, St Mary's Hospital, Praed Street, London W2 1NY. www.st-marys.org.uk/prion/
- 3: Professor Collinge at the MRC Prion Unit, Faculty of Medicine Imperial College, St Mary's Campus, Norfolk Place, London W2 1PG.
- 4: Professor Janet Darbyshire, MRC Clinical Trials Units, 222 Euston Road, London NW1 2DA www.ctu.mrc.ac.uk
- 5: Professor RG Will, National CJD Surveillance Unit, University of Edinburgh, Western General Hospital, Crewe Road, Edinburgh EH4 2XU. www.cjd.ed.ac.uk



In 1997 a specialist clinic for the assessment, investigation, diagnosis and ongoing management of all forms of prion disease was set up at St Mary's Hospital. The clinic staff includes consultant neurologists, a specialist prion therapist and a clinical nurse specialist.

Research

In March 2001 the Department of Health designated this service the National Prion Clinic with central funding. The clinic works closely with the Medical Research Council (MRC) Prion Unit, where there is an extensive research programme to develop ways of diagnosing prion diseases earlier and to develop treatments and ultimately a cure for these diseases. The research group has already developed tonsil biopsy for the specific diagnosis of variant CJD,

incubating variant CJD in the UK. This has already had major consequences for the health service with the introduction of measures to reduce the potential risk of person to person (secondary) transmission. Measures include leucodepletion (the removal of white blood cells) of all transfused blood and obtaining other blood products from outside the UK, an overhaul of hospital sterile services and introduction of single use instruments for some surgical procedures. The development of a

The National Prion Clinic at St Mary's Hospital, London

which now forms part of the established diagnostic criteria for this condition. To date everybody diagnosed through tonsil biopsy has had the disease confirmed at autopsy and all negative results have subsequently been found to have other conditions or have recovered.

It is now firmly established that variant CJD is caused by a BSE-like strain of the prion protein. Widespread exposure of the population to BSE prions has undoubtedly occurred. It is currently impossible to predict accurately the number of variant CJD cases that will arise: estimates range from hundreds to over 130,000. The possibility that a significant epidemic may occur in the next ten to 20 years cannot be ruled out at this stage.

There is also uncertainty about the number of people who may be

sensitive blood-based diagnostic test to detect prion infection is essential to manage this public health concern as it would allow early diagnosis. With a blood test it may be possible to screen donated blood and patients undergoing surgery to target risk reduction rather than rely on extremely costly global strategies as at present. The development of such diagnostics is a high priority within the MRC Prion Unit.

In addition, a major research programme is ongoing in collaboration with one of the large pharmaceutical companies to develop drugs to block the disease process. This is an ambitious research programme, but in our view essential. Progress to date, although at an early stage, has been encouraging. A number of existing drugs with potential disease modifying properties are also under

evaluation in animal models. If any of these prove to be effective in inhibiting the disease process in animals, clinical trials will be set up in order to assess their effectiveness in humans.

Quinacrine

There have been recent reports in the media about a possible treatment for CJD. These reports refer to an article in Proceedings of National Academy of Science (PNAS) in August last year by Korth et al (from San Francisco), which suggested that two drugs, quinacrine and chlorpromazine, block the production of the rogue form of prion protein. These studies were carried out in infected mouse brain cells cultured in a test tube in a laboratory. Quinacrine has not yet been studied in animals infected with prions. The authors suggest that the drugs be used as a treatment of prion disease. However, the evidence is very preliminary and further work needs to be carried out to establish whether the drugs are effective in humans.

As a result of this report hopes have been raised in patients and families. The Department of Health has asked the Medical Research Council (MRC) to fast-track the design of a clinical trial to evaluate the effectiveness of quinacrine (also known as Mepacrine) as a potential treatment for CJD. This is being carried out at St Mary's Hospital. Patients enrolled in the trial will undergo a variety of clinical and cognitive assessments which will determine whether quinacrine can inhibit the disease process.

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Fundraising in memory of my mother

Bairbre Ward

In November 1999, my mother became increasingly moody. She also complained she couldn't see properly, despite having new glasses. As the weeks progressed her mood swings became even worse. She put this down to her new HRT. She got very annoyed when she heard that her two older children wanted to come home for Christmas.

In February 2000, she was unable to work our new cooker without repeated instructions. She also got 'lost' walking home from a local acupuncture clinic.

In March she drove to collect my brother from school. However, she got out of the car to send a message and forgot where she parked it. She thought the car had been stolen and reported it to the gardai! She stopped driving soon after. She was becoming paranoid too. When she couldn't find things, she was convinced we were hiding them from her. When Mothers' Day came, she didn't even realise it was Mothers' Day and she had problems opening her presents. She locked herself in the bathroom (twice) and couldn't get out without prompting and instructions from the outside. The second time the bolt wasn't even across, she just couldn't push down the handle. Dad removed the bolt after that.

Mum's symptoms kept getting worse and Dad took her to A&E. They 'couldn't find anything wrong' and sent her home. He brought her back the following week, and, after a long wait in A&E, they admitted her. After many scans and tests the doctors

were beginning to have an idea. At first they suspected early onset Alzheimer's, but the rapidity of the progression puzzled them. She remained in hospital for a few weeks. Later, the idea of CJD came about. Dr Hutchinson (the consultant) asked for a family meeting. He told us he thought Mum had classical/sporadic CJD. Mum's prognosis was not good. We were asked if we wanted to take her home for a while. Dad did, but we managed just one month before we reluctantly agreed we couldn't manage anymore.

Mum was readmitted to hospital. At this stage she was incontinent and unable to care for herself. As the days went by, she couldn't swallow and was fed through an NG tube. Then her voice began to go and she couldn't speak. Time went by and she deteriorated further. The palliative care team was called in. They gave her a sub-cut infusion pump with morphine to make her comfortable and then arranged to have her transferred to the hospice. She moved there at the beginning of July.

In June 2001, I completed the Dublin Women's Mini Marathon in a time of 1 hour 26 minutes. Dad managed to get most of the sponsorship for me, and another woman, Nicola (who lost her brother-in-law to CJD), got all her family to sponsor me too. I managed to raise over IRE1,000 for the CJD Support Network.



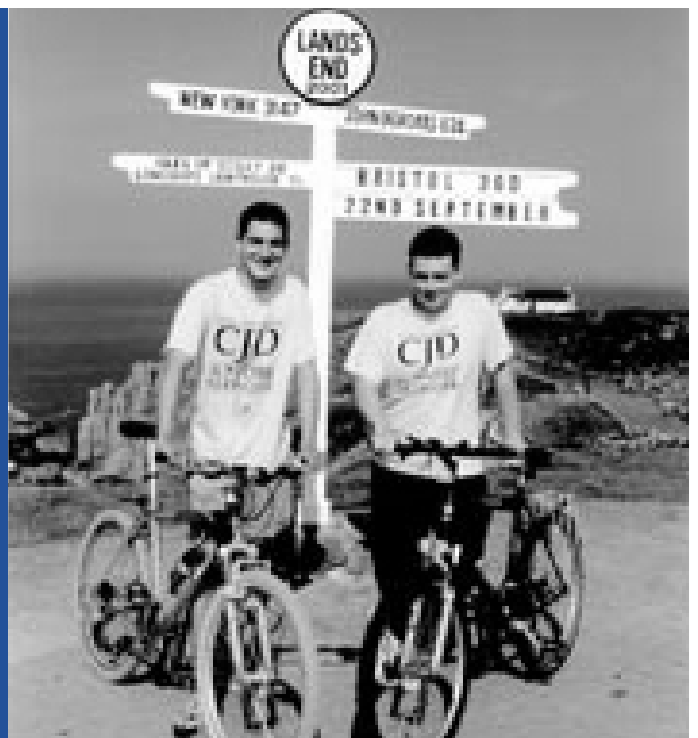
I hope to do the marathon next year. And if anyone wants to sponsor me they're more than welcome! I've already started training.

On 11 August I got a call at work from the ward sister at the hospice asking me to come in, telling me Mum wasn't at all well. However, she picked up and stayed pretty much stable for a week or so. On Sunday 20 August we had been to visit her. At 6.30pm we got a call from the hospice. She had died 15 minutes earlier.

A post mortem brain biopsy confirmed CJD. Just ten months after she started going 'crazy', my mother was dead. She was 56.

Cycle ride for CJD

In memory of Clair Tomkins who died with vCJD, her friends, Mark Ocock and Simon Burchell, organised a sponsored cycle ride. They rode 360 miles from Bristol down to Land's End using the national cycleway paths. The ride took six days in September and raised over £900 for the CJD Support Network.





Cliff Hyder and Rachael Bunning

Bunning jumps for CJD cash

Rachael Bunning's cousin, Cliff Hyder, was diagnosed last year with iatrogenic Creutzfeldt-Jakob disease (iCJD). He passed away on Monday 26 March 2001, aged 27, almost a year after the original diagnosis.

Rachael says that she was privileged to have been able to spend a lot of time with Cliff throughout his illness. She says, 'In fighting for more care and support for Cliff, I came to appreciate the lack of awareness of CJD in both the public and private sectors.'

I hope that through what we have learnt in caring for Cliff and the challenges we faced, and through the CJD Support Network,

it will be easier for people with CJD, their carers and the general public to find sources of information about CJD and obtain support. On 2 December I took part in a tandem parachute jump from 10,000 feet with the goal of raising £2,000 for the CJD Support Network and raising awareness about CJD.

Rachael says that after over five hours of waiting she was harnessed to Ken, a rather dashing skydive instructor. They hopped aboard the Black Beaver and she laughed hysterically as the plane climbed to 12,000 feet. 'There were a few seconds of sitting in the plane ... then dangling over the edge of the plane ... then smiling at the camera man ... and then I was face down staring at the Kent countryside that was getting closer and closer below me. While plummeting towards the ground it all seemed a bit surreal. I wondered if the air would suspend me should, well, anything go wrong!

'But then the parachute opened and for the remaining 5,000 or so feet Ken entertained me with his version of a parachute roller coaster....and I entertained our support crew on the ground who could hear me shouting all the way down!'



Dental treatment

Dear Editor

We spoke on the phone a few weeks ago about my son being refused dental treatment because his mother died of CJD. You referred me to Dr Andrew Smith at Glasgow Dental School. He was very helpful and I obtained a letter from Dr Richard Knight of the CJD Unit at Edinburgh.

The letter described in detail that my wife died of the sporadic form of the disease and that there was no good scientific reason for taking any particular precautions in providing dental treatment. This was the first letter I ever received confirming sporadic CJD. The death certificate merely specified cause of death as CJD.

The outcome was very good. My son sent a copy of Dr Knight's letter to his dentist and the dentist has now agreed to provide treatment.

Thank you for your help and the literature from the Support Network.

Yours sincerely,
Mr F Colley

Safe eating

Dear Editor,

I have visited your official website on CJD. It is a brilliant site that provides in-depth coverage on this most appalling disease. I am sure that your contribution to the public awareness on CJD can never be forgotten.

After reading all the articles on the site, there is one question remaining. That is, whether we could prevent ourselves from getting CJD if the beef is totally done. Are there any 'safety tips' for eating beef?

Thanks a lot.
Adrian Zhang

Palliative care research

Dear Editor

I am planning to start research into the palliative care needs of patients with vCJD in summer 2002. I am a doctor training in palliative medicine (hospice care) having previously worked in general practice. I have looked after a few patients with CJD in my role as a hospice doctor. In each instance I have been struck with how appropriate it was that the patient was under our care, although some hospices do not accept non-cancer patients.

In reading around the subject I have been surprised by how little has been written on how to care for someone with CJD. Research has focused on the pathological findings, investigation and diagnosis, at the risk of ignoring the physical and psychosocial needs of the patient and their carers.

Palliative care as a specialty has traditionally mainly looked after patients with cancer. However, there is much interest and increasing experience in widening palliative care to include any patients with a terminal progressive disease who have symptoms that need palliating (sorting out).

If you have personal or professional experience of caring for someone with vCJD, and have views on palliative care or my research, I would love to hear from you.

Yours sincerely

Dr Emma Jones

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Reiki and poetry

Dear Editor,

Our son Leon has only days to live now. It is tearing us apart with grief as you can imagine, but he has been receiving reiki healing from a reiki master three times a week for the past three weeks whilst he has been in a hospice. This has helped him, and us, enormously – it makes him calmer, brings down his temperature when his head gets very hot and he stays calm and cool. I feel sure reiki would help all those being nursed at present, and the fund is available for this. We all find too that often we have sat in the room whilst reiki is being given, we stay calmer for the rest of the day.

I am enclosing a copy of two poems that Leon wrote a few weeks before his diagnosis in May. I found them written on scraps of paper by his bedside. I think they explain the anguish our poor children experience before they are finally diagnosed.

Yours sincerely

Sandra Griffin

Editor's note: Since we received this letter and the poems, Leon Griffin has died. We offer the family our condolences

Poems written by Leon Griffin in April/May 2001

Poem 1

Let's touch an experience
For I've had a few
never been liked, loved or hated and
I'll never be happy what ever I do

To touch is to steal
If you feel it
Like I feel it too
I'll never be happy what ever I do

There's a face in the hallway
Mouthing out the words I knew
Shining cold for tomorrow
It's something bad, beautiful and forgotten
Whatever I do

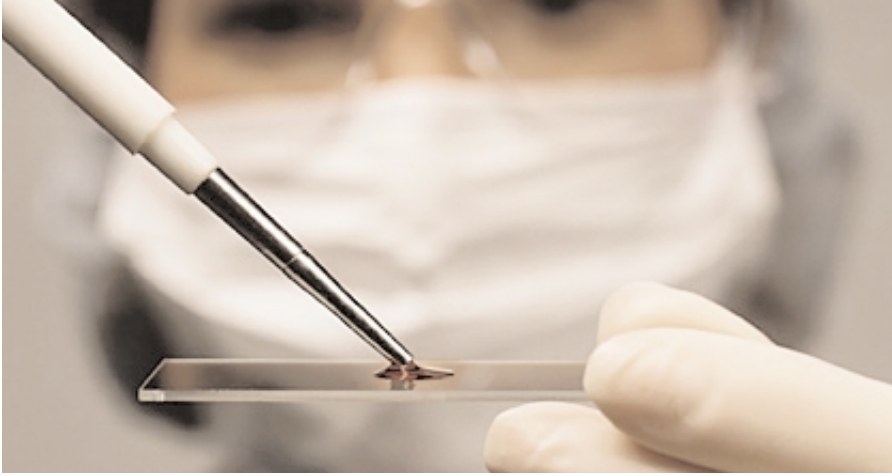
Poem 2

It's great being someone
Who has a headache
Like it's great being someone
You can touch but not take

It's fantastic watching
Your handwriting dissolved to this
fantastic listening to
your mind crackle and fizz

I want to forget all this and run
to where I do not know
The earth buries me deep
and it's not a game or a show

At the end of all beginnings
it stretches back and how
and I'm finding out to my cost
what it is to be taken now.



CJD research views

Missing immune gene may be implicated in CJD

The CJD Support Network welcomes the report in *Nature*¹ that suggests a missing immune gene may be implicated in vCJD.

This finding should help neurologists in the process of early diagnosis of vCJD and assist researchers in identifying potential drugs for treatment or prevention.

The research is small scale and needs confirmation by others. However, it appears to be another significant element in the complex jigsaw that constitutes vCJD.

1 HLA-DQ7 antigen and resistance to vCJD. *Nature* 414, 15 Nov 2001, pp 269. Collinge et al.

Limited epidemic?

French research on vCJD² suggests that the disease may have already peaked in the UK.

Dr Alain-Jacques Valleron and colleagues at the French National Institute of Health and Medical Research (INSERM) say that the vCJD epidemic may not be nearly as extensive as earlier studies have predicted.

Their analysis is based on a better understanding of the incubation period for vCJD and on evidence that young people are more susceptible to the disease. Using these factors a computer model has

been developed which suggests that the total number of vCJD cases will probably total about 205, with an upper limit of 403.

The CJD Support Network welcomes this new research but cautions that many uncertainties remain concerning this disease, which make accurate predictions difficult.

The overall numbers of people affected remain relatively low at 111 cases. We do not know the exact route of transmission of the agent nor do we know the size of an infectious dose. In addition there are genetic factors which relate to the disease that researchers are still investigating.

All cases of vCJD so far have copies of an MM gene which is present in 40 per cent of the population. It is still not known if an MV gene adds a protective factor against the disease or if it extends the length of the incubation period. If it is the latter then statistical predictions will need to be revised upwards.

It should be noted, however, that this research follows another recent prediction by Dr Huillard d'Agneaux and colleagues at the London School of Tropical Medicine and Hygiene that the total number of cases of vCJD are expected to be in the hundreds rather than thousands.

2 *Science*, 23 November 2001

Genetic susceptibility to prion disease

A study in *American Journal of Human Genetics*³ investigates genetic susceptibility to prion disease. The work is part of a major research programme addressing genetic susceptibility at the recently opened Department of Neurodegenerative Diseases and MRC Prion Unit at Queen Square, London. The idea driving the research is that genetic differences in the population may explain why some people get CJD and others do not.

We know that genetic differences between laboratory animals can affect the incubation time to prion disease – we want to find similar genetic differences in humans. Finding out about where the exact DNA codes are that make people susceptible to prion disease may help diagnose patients earlier and identify new strategies for drug development. A strong genetic factor is found in the DNA that encodes the prion protein itself, known as 'codon 129'. All patients with variant CJD have had one particular type of DNA, encoding a protein building-block called methionine at this genetic position.

The new research describes more than 50 new genetic differences near to codon 129. Some of these changes might affect the amount of prion protein that the body makes. One change in particular, known as 1368, was more likely to be found in patients with sporadic CJD than it was in the healthy population. There was no difference at the same position, however, between patients with variant CJD and the healthy population, but this might be because the numbers of DNA samples available were small. The

vCJD and blood

AN UPDATE

It simply isn't known yet if vCJD can be transmitted via blood. Until there's clear evidence either way the National Blood Service is taking every precaution to protect recipients

strength of the association is quite weak and does not yet lead to any useful diagnostic tests. Further work is underway to find out how the genetic differences affect susceptibility to prion disease.

3 Sporadic – but not variant – CJD is associated with Polymorphisms upstream of PRNP Exon 1. *American Journal of Human Genetics* 69, 000-000, 2001. Mead et al.

The link between BSE and vCJD

CJD Support Network's response to Dr George A Venters' theory about vCJD

The CJD Support Network is sceptical of Dr Venters' proposal that the link between BSE and vCJD is open to question⁴.

We understand that the pathological evidence available indicates that the brains of people who have died from vCJD have distinctive florid prion protein plaques surrounded by spongiform changes. These are very similar to the pathology of BSE.

The infection of people with vCJD which came to light in the mid 1990s can be closely correlated with the period ten years earlier (mid 1980s) when the UK population would have been most exposed to BSE in contaminated food.

Many families of people who have died from vCJD will view Dr Venters' theories with disbelief. Dr Venters' ideas need to be considered by epidemiologists and neuropathologists and responded to.

4 New variant CJD: the epidemic that never was. G A Venters. *BMJ* 323, 13 October 2001, p 858-861

The NBS has for many years screened each and every donation of blood. At present they test for hepatitis B and C viruses, HIV and syphilis. Another test we may be able to introduce in about two years' time is that for vCJD.

Although there is no risk to donors in giving blood, current scientific research indicates that there is an unknown risk that vCJD may be transmitted by blood and tissues. To date there is no evidence that this is the case, but our present state of knowledge suggests that it may be possible.

To minimise this unknown risk it is essential that the NBS carries out extensive research and risk assessment before any decisions are made.

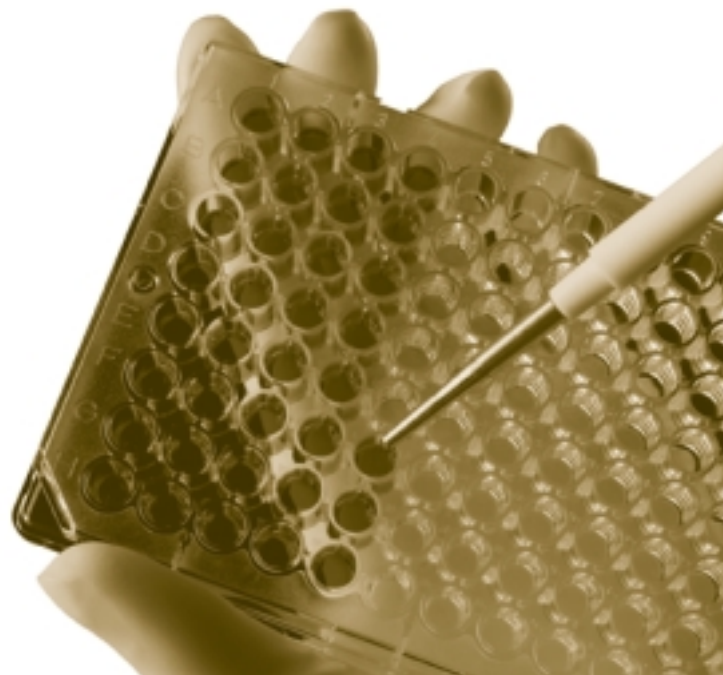
The NBS is committed to collaborating with experts who are working towards finding a test and any possible means of preventing vCJD from developing. It is encouraging to note reports on real progress being made in this area. The NBS has researchers involved in this quest, but equally important is the need for us to understand how best to handle the introduction of a test.

We introduced a couple of precautionary measures almost two years ago. First, the removal of leucocytes (white cells) from blood before it is transfused. This procedure is called leucodepletion.

You may have noticed our blood packs have an extra filter, which allows this process to take place back at our laboratories. The other measure introduced was the decision not to use UK plasma to manufacture blood products. For example Factor V111 for haemophiliacs. Plasma used for this process is imported from countries with no reported cases of BSE or vCJD.

vCJD presents major challenges to all blood services across the world, particularly in the UK. The NBS aims to keep people informed about future developments and would like to reiterate to all donors how vital their continued support is in helping to save and improve the lives of others.

Reprinted from *The Donor* (Autumn 2001) with the kind permission of the editorial team at the National Blood Service.



Dental treatment preferences

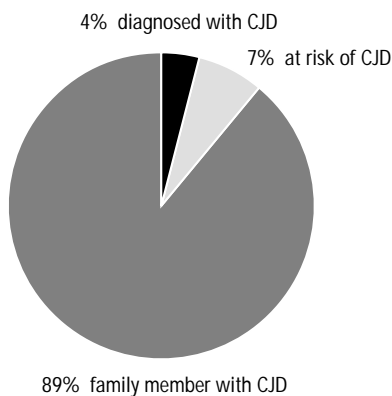
Results of the survey by the Glasgow Dental School of dental treatment needs for patients with or at risk from prion disease

Compiled by Dr Andrew Smith



Respondents

Figure 1: Present situation



The majority of respondents highlighted that they had a family member with CJD. This was the case for 89 per cent (n=50) of patients

Patients with a family member were asked what their relationship to this individual was

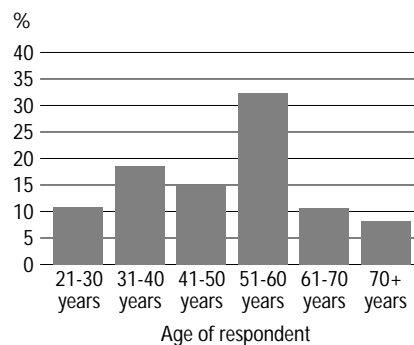
Figure 2: Relationship to person with CJD



Figure 2 highlights that 39 per cent (n=20) of patients stated they their relationship to the individual with CJD was parent.

The age of patients in the sample was as follows

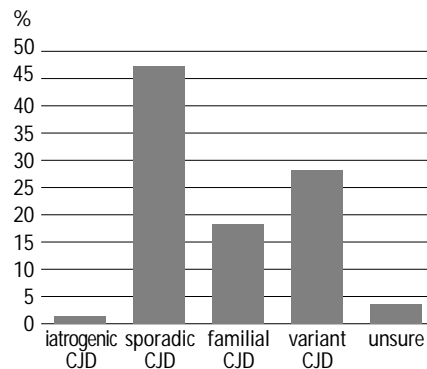
Figure 3: Time and day of attendance



Thirty-three per cent (n=16) of patients fell within the age band of 51-60.

Respondents were also asked which type of CJD either they or their family had. The following data was obtained:

Figure 4: Type of CJD

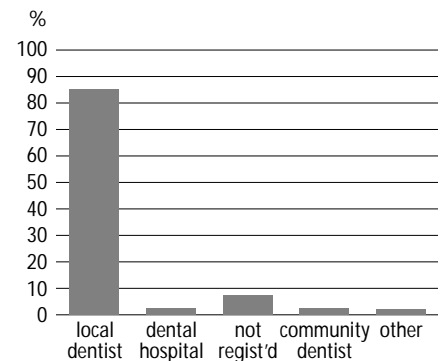


This graph highlights that almost half of respondents reported the type of CJD as being sporadic (n=24; 45 per cent).

Dental treatment

Respondents were asked where they currently attend for dental treatment.

Figure 5: Current location of dental treatment



It was evident from the data that the majority of patients (n=43; 86 per cent) attended a local dentist for treatment. In relation to this question, the following comment was made:

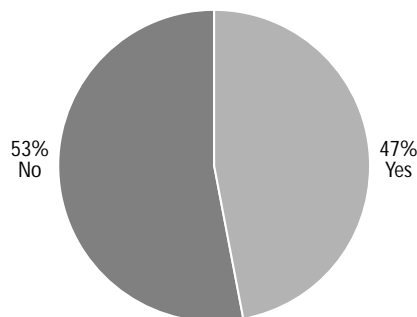
'We were registered with a dentist but after my husband died our dentist who was aware of the illness retired . The new dentist just kept us on for six months, only a check-up was offered and we were not offered to register with him. He made us feel very uncomfortable.'



Editor's note: The CJD Support Network and the Glasgow Dental School would like to thank the members who responded to this questionnaire circulated with the last newsletter.

In relation to this, respondents were asked whether they had informed the treating dentist of their medical history.

Figure 6: Medical history



This data highlighted that 53 per cent (n=26) of respondents had failed to inform the dentist treating them of their medical history. Respondents explaining why they had not informed the dentist provided the following reasons:

- Undiagnosed (n=4)
- Dentist did not ask/cover medical history (n=4)
- Never thought dentist needed to know (n=10)
- Not blood relation (n=1)
- Worried dentist would refuse to treat (n=1)

Respondents were also asked whether they or their family had been refused treatment as a result of their CJD status. It was clear from the data that very few respondents had encountered difficulty in accessing dental treatment. Indeed, only 6 per cent (n=3) of respondents had been refused dental treatment.

In addition, respondents were asked whether either they or their family had experienced problems in receiving dental care as a result of your CJD status. Only four (9 per cent) of patients responded affirmatively to this question. The following comments were provided as an adjunct to respondents' responses:

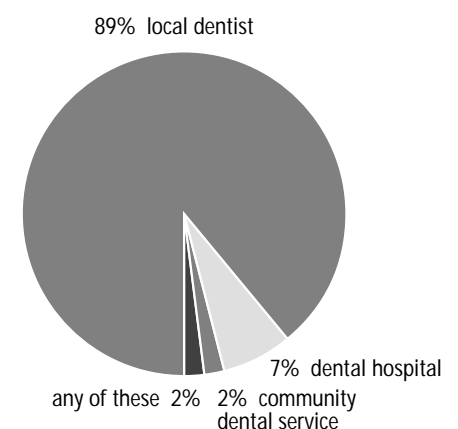
- 'At present we are having difficulties registering with a dentist and my children and myself need treatment. We have not seen a dentist since June 1999. Fortunately, having been in touch with the CJD Support Network I have some written information to take with me now in the hope of finding one.'
- 'Dental services informed and request made (through caring agency and physiotherapist). Long wait and requested home visit but service never materialised. Then my daughter died.'
- 'My dentist agreed to carry on treating me but would not let his hygienist treat me. He said all the equipment he used on me would have to be put in a bag with my name on it, so I had my own personal dental equipment. This has now been resolved, as he is now fully aware that CJD in the classical form is not passed on this way.'
- 'Our dentist had been treating us for some years when our son first became ill. He had not had any dental treatment for a couple of years. He didn't see the dentist whilst he was ill – it would have been quite difficult to get him there as the surgery was up two flights of

stairs. I am not aware there would have been a problem seeing the dentist and we have kept them informed of our son's condition. We have had no problems since.'

Respondents were asked whether they were aware of the current national guidelines disseminated to dentists regarding the management of patients with or at risk from CJD. Very few patients were aware of these guidelines. In total, only 29 per cent (n=14) of respondents were aware of such guidelines.

Finally, patients were asked where they would prefer to have their dental treatment carried out.

Figure 7: Dental treatment preference



It is clear from this graph that the majority of respondents (n=40; 89%) would prefer to have treatment carried out at a local dentist.

Who's who in the CJD Support Network



Bill Mitchell
Vice chairman of the network and a trustee of the Alzheimer's Society.



Gillian Turner National CJD case co-ordinator. Gillian acts as a link between network members, carers and professionals, co-ordinating care and answering enquiries on the helpline from a wide range of people.



Arthur Beyless
Treasurer of the network. Lost his daughter Pamela to vCJD.



Maria Byrne is a mother with three young children whose husband Graham had GSS.



Sarah Shadbolt
Sarah's husband died of classical CJD.



Penny Sinnott
Secretary of the Network. Penny's daughter Nina died of vCJD



John Williams
John's daughter Alison died of vCJD. John is a retired local government engineer.

Anita Tipping
Anita's son David died of CJD through growth hormone injections. Anita is a RGN at the Princess Royal MNH in London.



Kathryn Prout
Clinical nurse specialist at the Prion Unit, St Mary's Hospital London.



Dr Richard Knight
Consultant neurologist at the CJD Surveillance Unit.



Roger Tomkins
Richard's daughter Clare died of vCJD.

CO-OPTED MEMBERS

CJD Support Network membership application

The CJD Support Network is part of the Alzheimer's Society. Becoming a member of the Society 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 Alzheimer's Society's monthly newsletter.
 I would like to become a member but **not** receive the Alzheimer's Society's monthly newsletter.

There is no fixed subscription, but please give generously to help our work.

£8 £12 £25 £50 Other

Please make cheques payable to **Alzheimer's Society**

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

Name Title

Address

Postcode Telephone

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

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

CJDSN

CJD
SUPPORT
NETWORK

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

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