Fact sheet: Iatrogenic CJD

About the CJD Support Network

The CJD Support Network is the leading care and support charity for all forms of CJD. The CJD Support Network:

- Provides practical and emotional support to individuals, families and professionals concerned with all forms of CJD
- Provides emotional support to people who have been told that they are at a 'higher risk' of CJD through blood or surgical instruments
- Links families with similar experiences of all forms of CJD
- Offers financial support for families in need
- Provides accurate, unbiased and up-to-date information and advice about all forms of CJD
- Provides a national helpline on all forms of CJD
- Promotes research and the dissemination of research findings
- Promotes good quality care for people with all forms of CJD
- Encourages the development of a public policy response for all forms of CJD
- Provides support, education and training to professionals concerned with CJD

For more information about the activities of the CJD Support Network, contact:

Admin and general enquiries - admin@cjdsupport.net or +44 (0)7494 211476
Support - support@cjdsupport.net or 0800 774 7317
Website - www.cjdsupport.net
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Registered charity no. **1097173**

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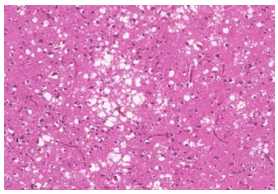
Introduction to iatrogenic CJD

Iatrogenic CJD (iCJD) is a form of Creutzfeldt-Jakob disease, which belongs to a group of rare, and always fatal, brain disorders called the prion diseases. This form of CJD arises from contamination with tissue from an infected person, usually as the result of a medical procedure or treatment.

CJD is caused by the accumulation in the brain of an abnormal form of a protein called a "prion protein". PrP can exist in two forms – normal (PrP^{C}) and abnormal (PrP^{Sc}). We all have normal PrP^{C} in our brain. The abnormal prion is different because it is folded in a different way and has a different shape to the normal one. Abnormal prion protein can cause normal prion protein to change shape and become abnormal. This leads to a chain reaction which, in turn leads to damage of brain cell.

Our first awareness of prion diseases

The first indication that human prion diseases might be transmissible through infected tissue came with the discovery of a disease called kuru among the Fore people of Papua New Guinea in the 1950s. Kuru mainly affected women and children, and began with unsteadiness of gait, shakiness and lack of co-ordination. Behavioural changes followed, although dementia was thought to be unusual (making it different from sporadic CJD; sCJD, for more information on sporadic CJD see the related fact sheet at www.cjdsupport.net). Eventually the patient would become unable to move and death would follow, usually within a year of onset of symptoms. The brains of these patients showed severe damage to the cerebellum, the part of the brain which controls movement. There were also spongiform changes (characteristic of prion disease) where the brain tissue has a spongy appearance when viewed under the microscope. A further feature was the appearance of small deposits called plaques within the brain tissue, distinguishing kuru from CJD, where plaques only occur in a minority of cases.



Microphotograph of spongiform change in brain tissue taken from a person with CJD.
Courtesy of Sebastian Brander, UCL

Kuru was eventually linked to the funeral rites of the Fore people, in which it was common for the women and children to handle the body of their dead relatives, including the brain and practice "endocannibalism" whereby the body was divided and consumed by kith and kin. Since the victims of kuru went on to be given these funeral rites, the disease perpetuated itself.

Transmission of CJD

Transmission of CJD by Surgery

Six people contracted CJD from brain operations with instruments, and investigations involving brain electrodes, which were previously used on someone with CJD. In these cases, the infection was delivered intracerebrally, that is, directly into the brain. The prion agent survives the disinfection procedures which normally destroy bacteria and viruses - but this was not known at the time. Now all instruments which have been used on the brain of someone with suspected CJD are destroyed. The incubation time for these intracerebral iatrogenic CJD varied from 18 to 46 months.

Transmission of CJD has also occurred with a corneal transplant on one occasion, with an incubation period of 18 months (with a possible second instance).

Grafts of dura mater, the tough membrane which covers the brain and spinal column, has been used in various kinds of surgery. Transmission of CJD via dura mater grafts has been reported in several countries, including the UK, but particularly in Japan. This is the commonest form of surgical transmission, with over 200 instances worldwide. For dura mater transmission, the incubation period has ranged from around 1 year up to many years.

It should be stressed that, with the exception of dura mater grafts, very few surgical transmission of CJD have been identified and precautions are taken where there is a known possibility of instrument contamination.

No instance of surgical transmission of vCJD has been identified.

Transmission with Human growth hormone

CJD has also been transmitted by treatment with human growth hormone. Human growth hormone, which is used to treat children with short stature, was prepared from human pituitary glands, its natural source, prior to 1985. Typically, 2,000 glands would be pooled to make one batch of growth hormone which, would be split into many hundreds of doses and distributed. Therefore, the inclusion of just one gland from someone with CJD had the potential to infect many people. 1,900 people have been treated with this form of growth hormone in the UK and there have been over 70 cases of iCJD (over 230 worldwide) arising from this cause. The incubation time for peripheral iatrogenic CJD is longer than for the intracerebral form, and is more like Kuru (itself a peripherally transmitted disease) being in the order of around 15 years, although recent cases have incubation times of 30-40 years. Growth hormone is now made synthetically, so there is no longer a risk of iCJD from this treatment.

Risk

Blood and Variant CJD (vCJD)

On the 17 December 2003, Health Secretary, John Reid, gave the news to the House of Commons that a patient had died of vCJD after receiving a blood transfusion from a donor who was subsequently found to have developed the disease (for more information on vCJD, see the related fact sheet at www.cjdsupport.net).

Since then, two further patients have died of vCJD as a result of contaminated blood. One other patient died of an unrelated condition, but on post mortem it was established that abnormal prion protein was present in the body, thought to be as a result of a blood transfusion. Another individual was found to have abnormal prion protein in the body, following their death from another cause. It is thought likely that they were infected via a blood product A treatment made from donated blood plasma).

It is now understood that blood may contain vCJD infectivity both in people clinically ill with vCJD and in those who are silently incubating the disease.

Risk through blood transfusion

As we do not know how many people who live in the UK are incubating vCJD and as there is no available validated screening test for blood, certain precautionary measures have been put in placeto reduce the risk of vCJD transmission via blood/blood products.

- Withdrawal and recall of any blood components, plasma derivates or tissues obtained from any individual who later develops vCJD (December 1997).
- Importation of plasma for fractionation to manufacture plasma products (announced May 1998, implemented October 1999).
- Leucodepletion-reduction of the white cell content- of all blood components-(announced July 1998, implemented Autumn 1999).
- Promotion of appropriate use of blood and tissues and alternatives throughout the NHS.
- People who have received a blood transfusion since 1980 are no longer able to donate blood.

It should be stressed that the few instances described above are the only ones identified to have resulted from blood/blood products, despite detailed

surveillance systems to detect any such transmissions. No instances have been identified for over 10 years.

When a person is diagnosed with CJD, their health history is examined to see if they have had surgery or donated blood in the past. The risk to public health is determined and anyone who is identified to be at an increased risk of contracting CJD, through for instance, a blood transfusion, is informed via their GP. Receiving this information, can be very distressing. Support and advice can be sought from the person's GP or agencies such as the CJD Support Network and those listed at the end of this fact sheet.

Risk through blood transfusion (continued)

Blood and Other forms of CJD

There are no confirmed instances of transmission of other forms of CJD by blood/blood products. There are reasons for believing it is a risk associated particularly with vCJD. Surveillance of possible blood transmission includes sCJD data.

Note on terminology

Clearly, transmission of vCJD by blood/blood products is a form of iatrogenic prion disease. However, for historical reasons, the term 'iatrogenic CJD' may be used by some to refer to only those instances of transmission of non-variant CJD through surgery, medical procedures or pituitary hormones.

Risk through organ transplant)

The risk of contracting CJD from organ transplants is uncertain, but believed to be small. A woman later shown to have been suffering from CJD did provide material for three eye operations (cornea and sclera). Unfortunately, a transplant usually has to be done before a full post mortem, so this risk cannot be completely eliminated, However, it will usually be known if a potential donor is suspected of having CJD. In the vast majority of cases, the benefit of having the transplant far outweighs the risk of CJD.

Ways CJD cannot be transmitted

It is important to realise that CJD is not infectious in the usual way -by airborne droplets, like colds and flu, or by skin contact, or by blood or sexual intercourse, like HIV. Therefore, there are no special risks from normal contact with a person with CJD.

Inherited risks

As with sporadic CJD, there appears to be a genetic predisposition to contracting iatrogenic CJD. We all have two copies of the PrP gene, one from our mother and one from our father. These copies can exist in two different forms; people who inherit two identical forms appear to be at greater risk. It may be that this form of PrP is more susceptible to changing into the abnormal form.

Symptoms of Iatrogenic CJD

Where transmission is intracerebral, the symptoms are like sporadic CJD:

Symptoms where transmission is intracerebral

- Initially, depression, memory lapses, maybe unusual fatigue. However, rapid progression to dementia and obvious neurological symptoms distinguishes CJD from depression.
- Within weeks, unsteadiness and lack of co-ordination. (Sometimes these symptoms are the first to appear)
- Sudden jerky movements, rigid limbs, maybe blindness and incontinence.
- Difficulty in speaking and swallowing.
- Eventually the patient loses the ability to move or speak, and will need full-time nursing care.

Symptoms in peripherally acquired iCJD

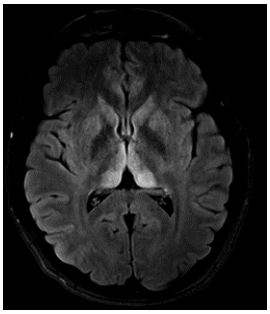
Peripherally acquired CJD is more like kuru:

- Symptoms of ataxia (unsteadiness and lack of co-ordination) predominating, and dementia being a rare feature.

Diagnosis

There is no absolute test for CJD. A definitive diagnosis is currently only possible by post-mortem examination of the brain for spongiform change. Plaques are commonly seen in growth hormone related CJD.

All GPs should be aware of CJD, although most of them will never have seen a case. A prompt referral to a neurologist should follow the reporting of any suspicious pattern of symptoms, where a number of investigations will be carried out including:



MRI scan of vCJD patient (Pulvinar sign) **Courtesy of National Prion Clinic, UCLH**

- Magnetic resonance imaging (MRI) This scan produces an image of the brain. It is mainly useful for ruling out other conditions such as a brain tumour. However, in some cases, a characteristic abnormality may be present, which aids diagnosis in all forms of CJD
- Electroencephalogram (EEG) may show characteristic changes present in non-specific brain disease
- Lumbar puncture. The presence of a particular proteins, particularly 14-3-3 in the cerebrospinal fluid, and the RT-QuIC test may be helpful in diagnosis.
- A brain biopsy (taking a sample of brain tissue) may be done to look for evidence of spongiform change, which would be diagnostic of sporadic CJD. This would only normally be carried out in highly selected cases, often to exclude CJD from a diagnosis or to confirm another potentially treatable illness.
- Blood and other biochemical tests. As at January 2008, there is no specific blood test for CJD

The diagnosis of CJD often takes time, due partly to the lack of a simple straightforward diagnostic test. It is also important to stress that a number of neurological conditions can look very similar in the early stages and, on occasions, it may be necessary to see how the illness develops over time before making a definitive diagnosis. In addition, clinicians do not wish to perform unnecessary distressing investigations on individuals. This time to make diagnosis can be a very distressing period for the family, particularly as their relative or friend may be deteriorating very rapidly. It is important that clinicians support families and friends through this difficult period and additional support is available from organisations such as the CJD Support Network.

Notification

The Chief Medical Officer has requested that individuals suspected of having CJD should be notified to two organisations, the National CJD Research and Surveillance Unit and the National Prion Clinic. Involvement with these research organisations is entirely voluntary for the patients and their families. Aside from their research functions, these organisations are able to provide additional information, help and advice.

Further information and contacts

Further information about CJD may be found on the CJD Support Network website at www.cjdsupport.net our fact sheets are also available by post on request to the Network.

Support and information may be obtained from the organisations below:

CJD Support Network	Admin and general enquiries - admin@cjdsupport.net or +44 (0)7494 211476 Support - support@cjdsupport.net or 0800 774 7317 Website - www.cjdsupport.net Post - PO Box 3936, Chester, CH1 9NG Registered charity no. 1097173
National CJD Research and Surveillance Unit	Western General Hospital, Crewe Road, Edinburgh EH4 2XU Website - www.cjd.ed.ac.uk 0131 537 1980 telephone number for general enquiries and loth.securecjd@nhslothian.scot.nhs.uk for Care Team enquiries/patient families
National Prion Clinic	National Prion Clinic, Institute of Prion Diseases, Courtauld Building, 33 Cleveland Street, London, W1W 7FF. Helpline for National Prion Clinic - 020 7679 5142 / 020 7679 5036 uclh.prion.help@nhs.net