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.co.uk or +44 (0)7494 211476
Support - support@cjdsupport.co.uk or 0800 774 7317
Website - www.cjdsupport.co.uk
Post - PO Box 3936, Chester, CH1 9NG

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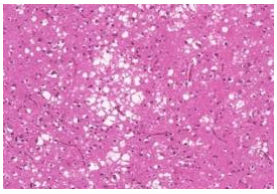
Table of Contents

Introduction

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 is the result of transmission of CJD from another person, usually via a medical procedure or treatment.

It is important to stress that while CJD can transmit from person-to-person, such occurrences are rare, and require special circumstances, as detailed below. Ordinary, even intimate, contact with someone with CJD is not a risk.

CJD is caused by the accumulation in the brain of an abnormal form of a protein called 'prion protein '. This protein can exist in two basic 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 cells.



Microphotograph os Spongiform change in brain tissue taken from a person with CJD
© Prof, John Collenge, MRC Nat. Prion Unit

Our first awareness of human-to-human transmission of prion diseases

The first indication that human prion diseases might sometimes be transmissible from person to person, 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 rather different from sporadic CJD). 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 particularly in the cerebellum, the part of the brain which controls the coordination of 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 kuru plaques, consisting of aggregated abnormal prion protein, within the brain tissue.

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 practise "endocannibalism" whereby the body was divided and consumed by their kith and kin, as part of their mourning process. Since the victims of kuru went on to be given these funeral rites, the disease perpetuated itself.

Transmission

By surgery

To date, 6 people have been identified as contracting CJD either from brain operations with instruments, or 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 survived the standard disinfection procedures which normally destroy bacteria and viruses - but this was not known at the time. Now all instruments which are known to have been used on the brain of someone with suspected CJD are destroyed. If instruments are used in brain procedures where the diagnosis might be CJD, they are quarantined until the diagnosis is clear. The incubation time (the time from exposure to developing symptoms) for these instances of 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. The dura mater was obtained from human cadvers and, in the past, some dura mater was obtained from people who had died of CJD. As a resuit, 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. There have been 8 dura mater-linked CJD cases in the UK, with the last identified person dying in 2005, and no UK cases identified since. 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 transmissions 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.

By human pituitary hormones

CJD has also been transmitted by treatment with human growth hormone (hGH), which is used to treat children with short stature, and, prior to 1985, was prepared from cadaveric human pituitary glands. 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, as of 2023, there have been 80 UK cases of iCJD (over 230 worldwide) arising . The treatment was given my intra-muscular infection and the incubation period is longer than for intracerebral transmission, often being in the order of around 15 years, although more recent cases have incubation times of 30-40 years.

Human Gonadotrophin (hGN), used in the treatment of infertility, was also prepared from cadaveric pituitary glands. Only 2 instances of hGN-CJD transmission have been reported, both relating to treatment given in Australia. Pituitary hormones are no longer prepared from cadervic pituitary glands, so there is now no risk of iCJD from this treatment.

Risk

Through blood transfusion & Blood Products

Three people have died as a result of transmission of vCJD through blood transfusions given between 1996 and 1999. Another individual died of a non-CJD illness and was found to have evidence of vCJD infection at autopsy; this infection is thought to have been via blood transfusion during the same time period. No further cases of vCJD transmission via blood transfusion have been identified, despite contionuing studies by the National CJD Research and Surveillance Unit and the UK Blood Transfusion Services.

Blood Products are medicinal treatments derived from the plasma component of donated blood. There is a single, probable instance of transmission of vCJD infection via one such product ('Factor VIII', used to treat Haemophilia). This individual died of a non-CJD illness and the infection was found at autopsy.

There is no identified instance of transmission of any form of CJD other than vCJD. There is a separate Information Sheet on blood and blood products on the CJDSN website.

Note on terminology
Clearly, transmission of vCJD, resulting in disease, 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.

Through organ transplant

The only definite documented instance of organ transplant realted CJD transmission is the corneal transplant instance detailed above.

The risk of contracting CJD from organ transplants is uncertain, but believed to be very small. Certainly, organ donation is not allowed from an individual thought to have CJD. Unfortunately, a transplant usually has to be done before a full post mortem of the donor, so a risk of unsuspected CJD cannot be completely eliminated, but this must be very small. 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 from person-person 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.

Genetic Factors

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. However, this genetic factor does not cause the illness; it is the unlikely chance of exposure to infection that is the cause.

Symptoms of Iatrogenic CJD

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

- Initial rather non-specificc symptoms, rapid progression to widespread brain symptoms, affecting memory and thinking, often with unsteadiness and inccordination.
- Speech, understanding and swallowing become difficult.
- Sudden jerky movements (called 'myoclonus') may be seen.
- Eventually the patient will need full-time nursing care.

Peripherally acquired CJD is more like kuru:

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

Diagnosis of Iatrogenic CJD

An absolutely definitive diagnosis of CJD is currently only possible by neuropathological examination of the brain. This is usually done at autopsy, although, in rare circumstances, a biopsy of the brain may be undertaken in life.

The diagnosis of iCJD is the same general process as for other forms of CJD, such as sCJD. The clue to a diagnosis of iCD is the history of a relevant past potential exposure, such as cadaveric-hGH treatment.

Details of diagnostic methods may be found in other CJDSN Information Sheets on our web-site. However, brain MR imaging and cerebrospoinal fluid analysis are key diagnostic tests.

The diagnosis of CJD often takes time and a number of neurological conditions can look very similar in the early stages; 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.co.uk 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.co.uk
Support - support@cjdsupport.co.uk or 0800 774 7317
Website - www.cjdsupport.co.uk
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
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