

Sporadic CJD

Sporadic CJD (sCJD) is one of the four different forms of Creutzfeldt-Jakob disease, which belongs to a group of rare, and always fatal, brain disorders called the prion diseases. These occur in both humans and animals, and include BSE. sCJD is also referred to as classical CJD.

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. 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.

Introduction to CJD

CJD was first described in the 1920s by two German neurologists (Creutzfeldt and Jakob). It causes a progressive loss of mental abilities and is accompanied by neurological symptoms such as unsteadiness and clumsiness.

The disease affects about one person in a million per year, giving rise to 50 or so new cases a year in the UK. Of these, 85 per cent are sporadic, having no known cause, with the remainder comprising genetic, iatrogenic and variant (see information sheets 2, 3 and 4). sCJD is most common in the 45-75 age group, with the peak age of onset being 60-65.



**Microphotograph of
spongiform change
in brain tissue taken
from a person with CJD**

At present, CJD can only be diagnosed for certain by post- mortem examination of the brain. Under a microscope, brain tissue from someone who had CJD has a characteristic spongy appearance, caused by numerous tiny holes where cells have died. For this reason, CJD, BSE and other prion diseases are sometimes called spongiform encephalopathies.

The cause of sCJD

Extensive research has shown no obvious cause for sCJD. Men are as likely to get it as women and there is no link with any particular occupation. Indeed, it occurs all over the world and it is important to emphasise that it is not thought to be related to BSE.

sCJD occurs with roughly the same frequency in all countries regardless of the occurrence of BSE in those countries. Individuals developed sCJD in the UK well before BSE was identified in cattle. There is also no known link between sCJD and scrapie (a disease of sheep). On present evidence there is no causal link between animal prion diseases and sCJD.

Abnormal prion protein the infectious agent

The infectious agent is thought to be a prion, an abnormal form of a protein called PrP. In its normal form, PrP occurs in the brain and other parts of the body in humans, a wide range of mammals and even in birds. The function of the normal PrP protein is unknown.

Unlike bacteria and viruses, prions are not inactivated by heat, ultraviolet light or other standard sterilisation procedures. When prions invade tissue containing normal PrP (PrP^C), they appear to convert it into the abnormal form (PrP^{Sc}) which leads to disease.

Vulnerability to this change can also be inherited, and it may occur for no known reason, as in sporadic CJD. Research has shown no firm link between the occurrence of CJD and any other risk factor, such as sex, occupation or diet. It occurs in countries such as Australia not known to be affected by BSE or scrapie, the sheep prion disease.

However, there is evidence that the majority of people with sCJD have a particular form of the PrP gene, which is found in only half the general population. This genetic variation may make normal PrP more vulnerable to conversion into the abnormal form associated with the disease.

The symptoms of sCJD

sCJD usually comes out of the blue, although the pattern of symptoms may vary from person to person.

- Early symptoms may be like those of depression – mood swings, memory lapses, social withdrawal and lack of interest. However, rapid progression to dementia and obvious neurological symptoms distinguish CJD from depression.
- Often within weeks the patient becomes unsteady on their feet, lacking in coordination, and markedly clumsy. This pattern of symptoms is known clinically as cerebellar ataxia, because it is caused by damage to the cerebellum – the part of the brain which controls movement. In some people, these are the first symptoms.
- Later symptoms may include blurred vision or even blindness, rigidity in the limbs, sudden jerky movements, and incontinence.
- Speech may become more difficult, or slurred. Swallowing may become difficult, and feeding by tube may eventually become necessary.
- Eventually the patient loses the ability to move or speak and they will require fulltime nursing care. In this state, known clinically as akinetic mutism, the patient's eyes can still move and they may appear to be following what is going on around them, but in fact they are not aware of their surroundings at this stage.
- The average duration of the disease is 4–5 months; 70 per cent of patients die within six months of the onset of symptoms and some within a few weeks. Rarely, sCJD patients survive for several years. It is thought that most people with CJD eventually lose insight into their condition.

Diagnosing CJD

As at January 2008, there is no absolute test for 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:

- 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. In sCJD the scan usually looks normal. However, in some cases, a characteristic abnormality may be present. A computerised tomography (CT) scan of the brain is usually normal.
- Electroencephalogram (EEG) often shows a characteristic change in the brain waves in sCJD.
- Lumbar puncture. The presence of a particular protein called 14-3-3 in the cerebrospinal fluid is very helpful in the diagnosis of sCJD. The increased level of this protein is caused by the rapid loss of brain cells.
- 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 and help to confirm the diagnosis

The diagnosis of CJD often takes time, due principally to the lack of a simple straightforward diagnostic test. It is important to stress that a number of neurological conditions can look very similar in the early stages and it is important, on occasions, 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 that additional support is available from organisations such as the CJD Support Network.

Treatment for sCJD

At present (January 2008), there is no proven treatment for CJD. However, there are a number of possible treatments being investigated in the laboratory. One potential treatment, Quinacrine, has been assessed (Prion-1 Trial funded by the UK Medical Research Council and co-ordinated by the London National Prion Clinic). Entry into this trial ceased on in 2006.

Another possible treatment, Pentosan Polysulphate (PPS), has been given to a number of CJD patients on an individual basis. This needs to be administered directly into the brain and therefore the treatment involves a neurosurgical operation. The Medical Research Council (MRC) commissioned a review of these individuals who have received PPS. Further information about possible treatment development can be obtained from the MRC and the National Prion Clinic.

There are a number of drugs which can relieve some of the symptoms of sCJD and make the patient more comfortable – for example, treatments for psychiatric symptoms, pain and the jerking movements.

Support and care

General support and care for the patient, family and friends is equally important. Social services should be involved in an early stage to advice on financial matters, respite and long term care. Various therapists – including speech and language therapists, physiotherapists and occupational therapists – will provide help with specific problems. Community nursing may provide more general nursing care outside hospital. There is now a national care package based at the National CJD Surveillance Unit in Edinburgh providing advice and support for individuals with CJD, their families and also local health professional. The national care package provides help with organising care and in certain circumstances, with funding of this care.

What happens on admission to hospital varies. Much depends on the type of hospital, the particular type of patient and the views of the family. Following admission there will be investigation and tests to establish the diagnosis and general supportive care.

Notification of sCJD

The Chief Medical Officer has requested that individuals suspected of having CJD should be notified to the National CJD Surveillance Unit and the National Prion Clinic. Involvement with these 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.

Research

There is much research underway into the causes of CJD and potential treatments. For instance, it may be possible to develop drugs to stop the conversion of normal PrP into abnormal prions, or to turn off the PrP gene. The function of PrP is unknown and laboratory animals have been shown to survive quite well without it.

Glossary

Cerebellar ataxia	Shaky movements, unsteady gait and clumsiness caused by damage to the cerebellum – a part of the brain which controls movement and balance.
Myoclonus	Jerking movements of the limbs caused by sudden muscle spasms.
Akinetic mutism	A state of complete physical unresponsiveness caused by damage to the base of the brain.
Spongiform change	Brain damage characterised by a spongy appearance of brain tissue seen under a microscope.
Encephalopathy	Any disease in which the overall functioning of the brain is impaired

Further information and Contacts

Further information about CJD may be found on the CJD Support Network website at www.cjdsupport.net and in the booklet “CJD and Prion Disease” obtainable on the website and from the Network.

Support and information may be obtained from the organisations below.

CJD Support Network
Helpline: 01630 673 993

CJD Support Network
Gillian Turner
National CJD Co-ordinator
CJD Support Network
Po Box 346
Market Drayton
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Tel/fax 01630 673 993
www.cjdsupport.net
Email Info@cjdsupport.net

National Prion Clinic
Po Box 98
National Hospital for Neurology
and Neurosurgery
Queen Square
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Tel 0207405 0755 (direct line)
Fax 020 7061 9889
www.nationalprionclinic.org
email help.prion@uclh.org

National CJD Surveillance Unit
Western General Hospital
Crewe Road
Edinburgh EH4 2XU

Tel 0131 537 1980 (Pathology)
Tel 0131 537 2128 (Clinical office)
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