

Fact sheet: Sporadic 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

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Registered charity no. **1097173**

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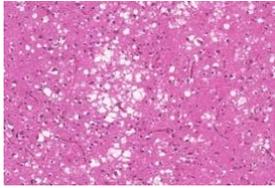
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Introduction to CJD



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

Courtesy of Sebastian Brander, UCL

Sporadic CJD (sCJD) is the commonest of the four main types of Creutzfeldt-Jakob disease (CJD). CJD is one of a group of rare brain disorders called the prion diseases (which affect animals and humans). Under the microscope, brain tissue from a person or animal with a prion disease, typically shows a characteristic spongy appearance, caused by numerous tiny holes where cells have died. For this reason, CJD and other prion diseases are sometimes also called spongiform encephalopathies.

CJD was first described in the 1920s, by Dr Jakob and the disease was then associated with Dr Creutzfeldt, giving rise to the name still used today. CJD is, as other human prion diseases, characterized by the accumulation in the brain of an abnormal form of a normal protein (prion protein)-giving rise to the term 'prion disease'. Prion protein (PrP) can exist in two main forms – normal (PrP^C) and abnormal (PrP^{Sc}). We all have normal PrP^C in our brain, although its exact functions are not entirely clear. The abnormal protein is different because it is folded in a different way, producing a different shape that has different physical and chemical properties. Abnormal prion protein can cause normal prion protein to change shape and become abnormal, leading to a sort of chain reaction producing increasing amounts of PrP^{Sc}. Because of its different properties, PrP^{Sc} aggregates and is deposited in brain tissue. This protein abnormality is associated with progressive damage to neurons (brain cells) and this gives rise to neurological problems, including a progressive loss of mental abilities, accompanied by a variety of other symptoms.

CJD has been divided into four main types, essentially relating to cause. Genetic CJD results from a faulty gene. Iatrogenic CJD results from accidental transmission of CJD via medical or surgical procedures. Variant CJD arose from contamination of diet with BSE from affected cattle. Sporadic CJD accounts for over 80% of CJD and is so called as it occurs sporadically and randomly in the population without clear cause. A general factsheet on prion disease, as well as individual information on the different forms of CJD can be accessed [here](#).

Sporadic CJD (sCJD)

What is it?

Accounting for around 80% of human prion disease, sCJD is the commonest of the four forms described above. The term 'sporadic CJD' reflects the fact that the disease occurs sporadically and randomly throughout a population.

There are around 1-2 deaths per million of the population per year in all countries where studies have been undertaken. No country appears to be affected particularly. In the UK, in recent years, there have been around 125 deaths per year. In the past, sCJD has sometimes been referred to as 'classical CJD'.

As described above, it is a disease characterised by a protein abnormality and associated dysfunction and death of neurons (brain cells). In this respect, it is similar-in pathology- to some other diseases such as Alzheimer's Disease (AD) and Parkinson's Disease (PD); in these, there is also a protein abnormality, but affecting different proteins to the prion protein. All these protein misfolding diseases affect mainly those in middle-age to later life, and cause progressive brain dysfunction. As a group, they have been termed 'neurodegenerative diseases'. However, sCJD is much rarer than either AD or PD and the illness generally progresses much more rapidly.

What causes sCJD?

The cause of sCJD remains unknown, despite extensive research. However, current opinion is that it represents a random error somewhere in prion protein production that leads to PrP^{Sc} formation and then on to neurological disease. In other words, it is thought to be the result of a biological mistake in the body that has devastating consequences-similar to how a mistake in cell production can produce cancer. Given the huge number of protein molecules that the body is making constantly, errors in production may occur. There are 'quality-control' systems that deal with abnormal proteins, but these may not be totally effective, perhaps especially as the body ages.

While research has failed to identify a definite cause, certain risk factors are known. Risk factors for a disease are things that increase the likelihood of an individual getting that disease but which are not, in themselves, a direct cause. The two most important of these for sCJD are age (as mentioned above) and genetic make-up:

- CJD is exceptionally rare in the young but becoming increasingly common with age; the peak age of onset being 60-65. The reason for this association with ageing is not known for certain. However, as mentioned above, other neurodegenerative diseases associated with abnormally folded proteins in the brain are also typically diseases of ageing. [There is, in fact, a noted fall in the incidence of sCJD in the very elderly. It is not known if this reflects under-diagnosis in that age group, a real fall that is not understood, or both].
- We all make normal prion protein (PrP^C) and the instructions for protein manufacture are contained in genes. The gene responsible for prion protein in

humans is called *PRNP*. Disease-causing mutations in this gene are responsible for genetic CJD. As is true for genes in general, there are common variations in the code sequences in *PRNP* that are generally harmless variations and ones that do not directly cause disease. However, one particular variation, whilst not directly causing disease, affects one's likelihood of developing sCJD. This is referred to as the *PRNP*-129 polymorphism. All individuals are either 129-MM, 129-MV or 129-VV. Being 129-MM is a risk factor for and being 129-VV is a partial protection against developing sCJD. It should be emphasized that, while this is an established important fact, at an individual level it is not a matter for anxiety: about a third of the UK population are 129-MM and very few of them ever develop sCJD.

Men and women are affected equally and there is no link to particular occupations.

sCJD, vCJD and BSE

It should be stressed that sCJD is not due to BSE. It was recognised long before the cattle BSE epidemic, and is found in all countries, at similar rates, regardless of whether those countries were affected by BSE. There are important differences in the clinical picture, medical investigation results and pathological characteristics between sCJD and vCJD (the form of CJD related to BSE). Unfortunately, sCJD and vCJD are sometimes confused by individuals and the media.

Is sCJD becoming commoner?

The UK annual mortality rate for sCJD has increased, relatively steadily, over the period 1990-2022, from around 0.5 to 2.0 deaths/million of the population/year. Although it is difficult to prove, it is considered that this increase is not a real increase in people affected, but rather due essentially to increased awareness/recognition of the disease and to much better diagnostic techniques.

While it has been proposed that the increase in UK sCJD cases might possibly be due to some cases actually being due to BSE, there is no good evidence to support this. Similar increases in sCJD have been seen in other countries with comparable CJD surveillance systems, regardless of whether or not those countries had BSE cattle.

Is sCJD transmissible?

As discussed above, sCJD is not thought to be acquired as an infection, but thought to be due to some random biological error. It is, however, potentially, transmissible from person-to-person, but only by very specific means. Such transmission from sporadic CJD has occurred very rarely, relating to specific forms of surgery and to the past use of certain body tissue materials; this results in 'iatrogenic CJD' and more detailed information on this is provided in a dedicated fact sheet which can be accessed [here](#).

There is no proven instance of sCJD being transmitted by blood transfusion. Most importantly, there is no risk from ordinary (even intimate) contact with someone suffering from sCJD.

How does sCJD affect people?

Early Symptoms

These are relatively nonspecific (such as social withdrawal, mood changes, sleep disturbance, dizziness, unsteadiness, forgetfulness etc) and so could suggest a wide range of possible diagnoses from minor transient illnesses, through anxiety or depression, to the beginnings of a number of neurological diseases.

Later features

As the disease develops, mental impairment becomes more obvious and often unsteadiness and incoordination. Visual and speech problems are not uncommon.

Late features

The illness eventually causes major neurological impairments leading to severe mental impairment, loss of mobility, loss of speech, impaired swallowing, incontinence and immobility. In many cases, sudden jerking movements are seen (called myoclonus). Loss of vision or even blindness may occur. Most individuals lose awareness or insight in the later stages and therefore their condition may be more upsetting to others than themselves.

Progression

In many cases, the progression is rapid. The average duration of the disease from onset to death in the UK is 4–5 months; over two thirds of patients die within six months of the onset of symptoms and some within as short a time as few weeks. In many instances, this rapid progression means that medical investigation needs to be undertaken on an urgent or semi-urgent basis; care and support plans need to be implemented and adjusted rapidly.

Although the above describes the typical situation, sCJD can be a varied illness and some individuals follow unusual courses. For example, some individuals have rather more slowly progressive problems and, rarely, they may live for 1-2 years or more. Some individuals present with a single symptom (for example visual loss or loss of balance) without other difficulties and sCJD is not the obvious cause—other illnesses being far more likely.

Diagnosing sCJD

It takes time & there are other illnesses to consider.

The first important aspect of diagnosis is that the presentation of sCJD is generally non-specific and all of the clinical features can occur in other diseases, which are often more common than sCJD and may, unlike sCJD, be treatable. Therefore, clinicians need to undertake a number of medical tests so as not to miss other possible diagnoses.

In addition, one important aspect of an illness is that the way it evolves and clinicians sometimes need to see how things change over time in order to make or confirm a diagnosis. Clinicians also do not want to undertake potentially distressing tests if they can be avoided. As a result, the diagnosis of sCJD can take time and it is important that patients and families receive appropriate explanation and support during this difficult uncertain time—from their clinicians and from additional sources such as the CJD Support Network.

Tests typically undertaken

- Many blood tests (and other tests such as a chest X-Ray etc) may be undertaken in relation to other possible diagnoses.
- Brain imaging is undertaken as a routine in most brain diseases. CT and/or MRI might be undertaken but MRI is the most useful investigation in this context. This is often done in the first instance in relation to other possible illnesses. However, the MRI may show abnormalities that are particularly suggestive of sCJD and these may either raise the first suspicions of sCJD or help to support an already suspected diagnosis.
- An EEG (electroencephalogram: recording the electrical activity of the brain) may be undertaken for various reasons. In some cases, it can show an abnormality that is suggestive of sCJD. It is an investigation that is not always undertaken.
- A lumbar puncture is usually performed. A needle is inserted into the lower back to obtain CSF (cerebrospinal fluid—a clear fluid that surrounds the brain and spinal cord). This is often done in the first instance to look for evidence of other, for example inflammatory, diseases. However, certain special tests can be undertaken on the CSF in relation to sCJD:
 - (i) Analysis for two proteins (14-3-3 and S100b); in most (but not all) cases of sCJD, the 14-3-3 test is positive and the S100b level is raised.
 - (ii) The RT-QuIC test.. In around 95% of cases of sCJD, the RT- QuIC test is positive.

Tests: some comments

- It is important to emphasise that the tests undertaken have two roles: firstly, to look for evidence for other (non-sCJD) illnesses and, secondly, to find abnormalities to support the diagnosis of sCJD.
- The tests showing abnormalities that have been in longest use (EEG, MRI and CSF 14-3-3/S100b) are essentially non-specific. In other words, they do not rely on the fundamental prion disease process and the abnormalities seen, while characteristic of sCJD, may be seen in other diseases. Positive results, therefore, always need careful evaluation in the whole clinical context. Nonetheless, if being viewed by an experienced clinician, in the correct context, they may be very helpful indeed. For example, given a clinical picture suggestive of sCJD, in the absence of evidence for any other illness, a combination of typical MRI appearances and a positive CSF 14-3-3 test, make a diagnosis of sCJD highly likely.

- The CSF RT-QuIC test is based on the underlying prion protein abnormality and is, therefore, a highly specific test. Having excluded other relevant diagnoses, a positive CSF RT-QuIC makes the diagnosis beyond reasonable doubt (as of February 2022, the UK CSF laboratory has not found a positive CSF RT-QuIC in anyone who proved to have another illness).
- However: all of the above tests can be negative in some cases of sCJD; negative or normal tests may lower the probability of the diagnosis but cannot, in themselves, absolutely exclude it.
- And: currently, the only method of absolutely definite diagnosis is demonstrating disease-specific abnormality in brain tissue by a neuropathologist. Brain tissue can be obtained through brain biopsy in life but this only rarely undertaken and for very specific reasons. Brain tissue, if obtained, is usually obtained at autopsy.
- There are other tests under development that are not yet in widespread clinical use. For example, material obtained from brushing the upper part of the inside of nose has been used in one test. There is, however, no blood test yet developed for sCJD.

Medical treatment for sCJD

At present (February 2022), there is no proven treatment that cures or slows progression of sCJD. However, there are a number of possible treatments being investigated in the laboratory. Please see our separate information on treatment research

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 distress, agitation, pain and the jerking movements.

Support and care for sCJD

Although there are no curative treatments, general support and care for the patient, family and friends is obviously important. Social services should be involved in an early stage to advise on financial matters, respite and long-term care. Various therapists – including speech and language therapists, physiotherapists and occupational therapists – can provide help with specific problems.

Community nursing may provide more general nursing care outside hospital. There are Specialist nurses and doctors based at the National Prion Clinic (NPC) in London and the National CJD Research and Surveillance Unit (NCJDRSU) in Edinburgh who can provide support, advice and education to patients, families and local care professionals.

There is a National Care Package administered by the NCJDRSU to help provide additional support for individuals with CJD.

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.

Research

There is much research underway into the causes of CJD and potential treatments. The involvement of patients and families with the NPC and NCJDRSU is invaluable in this research. Please see our separate information on research.

Notification

The Chief Medical Officer has requested that individuals suspected of having CJD (including sCJD) should be referred to the National CJD Research & Surveillance Unit and the National Prion Clinic. These units will try, when possible, to visit all referred patients and their families but 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.

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

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