SPORADIC CJD

Sporadic CJD (sCJD) is the commonest of the four main types of Creutzfeldt-Jakob disease (CJD). CJD is one of a group of rare, and always fatal, brain disorders called the prion diseases (which affect animals and humans). sCJD has sometimes been referred to as classical CJD. 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.

Introduction to CJD

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). 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 function is 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 biological 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 abnormal protein accumulation is associated with progressive damage to 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 and has been found in many countries at about the same frequency. There are around 1-2 deaths per million of the population per year in all countries where studies have been undertaken. In the UK, this amounts to around 110 per year.

CJD as an infection

Two forms of CJD (iatrogenic and variant) are acquired by infection. The infective agent involved in such prion diseases is termed the 'prion'. Its precise nature has not yet been determined but its nature and behaviour is quite different from that of the usual infective agents (such as bacteria and viruses). It is thought generally to be composed entirely or mostly of the abnormal form of prion protein (PrP^{Sc}).

Genetic forms of prion disease and sporadic CJD are not considered as acquired infections. However, there is a risk of their being accidentally passed on to others as infections. For example, iatrogenic CJD is thought to have arisen from contamination of medical products or instruments by material from sporadic (or possibly genetic) CJD affected individuals. However, it should be stressed that such transmission from sporadic CJD has occurred rarely and only through very specific means; there is no risk from ordinary (even intimate) contact with someone suffering from sCJD.

The Cause of sCJD

Extensive research into sCJD has failed to identify a definite cause; the current general view is that arises spontaneously in an individual, perhaps because of a random error in the prion protein, during its production or functioning. It occurs all over the world, at about the same rate and it is important to emphasise that it is not related to BSE dietary contamination. sCJD occurs with roughly the same frequency in all countries regardless of the occurrence of BSE in those countries and was recognized many years before the occurrence of the cattle BSE epidemic. There is also no known link between sCJD and scrapie (a disease of sheep and goats). Overall, on present evidence, there is no causal link between any animal prion diseases and sCJD. Men are as likely to get it as women and there is no link with any particular occupation.

However, 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 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, other neurological diseases associated with abnormally folded proteins in the brain (such as Parkinson's Disease, Motor Neuron Disease and Alzheimer's) 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.

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 somes 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. These are, firstly, analysis for two proteins (14-3-3 and S100b) and, secondly, the RT-QuIC test. In most cases of sCJD, the 14-3-3 test is positive and the S100b level is raised. 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 January 2018, 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 (January 2018), 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 (NCDRSU) 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.
The CJD Support Network is, of course, committed to providing additional advice and support at all times.

UK National Referral System

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.

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 researc

Further Information and Contacts

Further information about CJD may be found on the CJD Support Network website at *www.cjdsupport.net* and also by post on request to the Network.

Support and information may be obtained from the organisations below.

CJD Support Network

CJD Support Network Helpline: 0800 0853 527
CJD Support Network Website
Twitter
Facebook
Address
Email

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
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National CJD Research & Surveillance Unit
The Bryan Matthews Building
Western General Hospital, Crewe Road
Edinburgh EH4 2XU

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National Prion Clinic
National Hospital for Neurology and Neurosurgery
University College London Hospitals NHS Foundation Trust, London
MRC Prion Unit at UCL
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Courtauld Building
33 Cleveland Street
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