



CREUTZFELDT-JAKOB DISEASE – FACTSHEET

What is CJD?

Creutzfeldt-Jakob disease (CJD) is a rare, neurodegenerative condition characterized by rapidly progressive dementia and a variety of other neurological symptoms including unsteadiness and involuntary jerking movements. Brain pathology reveals characteristic spongy changes with numerous tiny holes seen under the microscope – so called spongiform change. CJD is a human form of prion disease. Prion diseases also occur in animals, e.g. BSE in cattle, scrapie in sheep. Most prion diseases are transmissible under specific laboratory conditions and the infectious agent is believed to be the abnormal protein, the prion, rather than a bacteria or virus. We all have prion proteins in our brain but it is believed CJD occurs when the normal prion (called PrP^C) is converted to an abnormal, more resistant form (PrP^{Sc}).

There are four distinct types of CJD and each will be described in turn.

Sporadic CJD

This affects around 60 people in the UK each year (1 – 1.5 / million) and is seen all over the world. The cause is unknown and there is no known link with BSE. It typically begins in late middle age but cases as young as 14 and as old as 90 have been recognised. Early symptoms include forgetfulness, unsteadiness and visual disturbance. Characteristically it progresses rapidly with dementia, involuntary jerks (myoclonus) and ultimately the person is bedbound and may not be able to speak. Typically the illness lasts only 4 to 6 months and death is often due to pneumonia.

Variant CJD

This was first described in 1996 and there is good evidence linking it to BSE from cattle, probably by eating infected foodstuff. It is very rare with only 174 cases worldwide,

most of which are in the UK. It affects younger people than sporadic CJD does, typically beginning in the late 20s. It also has a longer duration with most cases surviving around a year. Clinically it looks different to sporadic CJD, often beginning with psychiatric disturbance such as depression and anxiety, or uncomfortable sensory symptoms, before dementia, balance problems (ataxia) and involuntary movements set in. Variant CJD brain pathology shows unique florid plaques as well as the usual spongiform change seen in other CJD types.

Genetic CJD

This is the inherited form of CJD, caused by a mutation or coding error in the prion protein gene. Around 5 cases are identified each year in the UK. The inheritance pattern is autosomal dominant, meaning it is passed directly from one or other parent to the child. Each child has a 50% chance of inheriting the gene defect. Although one would expect all genetic cases to have a family history of CJD this is sometimes not the case. Possible explanations include the parent not being diagnosed or dying first of something else, or a case arising because of a new mutation. Genetic CJD usually presents in a similar manner to sporadic CJD, but often begins slightly earlier (e.g. in the 50s) and the illness lasts rather longer. However, the exact clinical picture depends on the specific genetic mutation.

Iatrogenic CJD

This refers to CJD caused by inadvertent transfer of infected material during medical procedures. Causes include human dura mater grafts, pituitary derived human growth hormone injections, corneal grafts and neurosurgical instrumentation. The delay between the procedure and developing CJD can be as long as 27 years. Dural graft cases usually look like sporadic CJD whereas growth hormone cases tend to present with balance problems and less dementia.

Investigations

A variety of tests are used to help diagnose CJD

- MRI (magnetic resonance imaging) brain scan, this is performed to exclude other diseases that may mimic CJD and to look for specific signal changes which are seen, particularly with variant CJD and sporadic CJD.
- EEG (electroencephalogram) – this involves placing electrical leads on the scalp to measure brain waves, and is especially helpful in sporadic CJD where a particular pattern is often recognised.
- Lumbar puncture – a needle is inserted into the base of the spine under local anaesthetic to obtain cerebrospinal fluid (CSF). This is analysed to exclude infection and inflammation, and to identify a protein called 14-3-3 which is frequently elevated in CJD.
- Blood test to sequence the prion protein gene – this can confirm or exclude genetic CJD and is recommended in most cases of CJD to rule out hereditary disease. Multiple other blood tests are usually done to exclude other causes of dementia and unsteadiness.
- Tonsil biopsy – this is only helpful in variant CJD and typically shows evidence of disease associated protein.

Unfortunately none of these tests can completely confirm or exclude the diagnosis but help provide further evidence to support it. A definite diagnosis of CJD requires brain tissue to be examined pathologically. This is usually taken at the post mortem but occasionally a brain biopsy is performed in life under a general anaesthetic.

General points – transmission, treatment and support for families

CJD is not infectious in the way that flu or a cold is, so family members and others do not need to be concerned about touching and hugging their relative. However, we know there is a transmission risk via contaminated surgical instruments and also blood transfusion in the case of variant CJD. Therefore the clinician is advised to inform the local public health team of a suspected case of CJD.

Sadly there is no cure for CJD and most treatment is purely symptomatic (eg sodium valproate to damp down myoclonus, sedatives to treat insomnia and agitation). However, new drugs are being investigated.

One potential treatment, quinacrine, is being assessed in the MRC Prion-1 trial. Another drug, pentosan polysulphate has been given intraventricularly to a small number of prion disease patients. As yet there is no convincing evidence that any treatment reverses or even significantly slows the disease. General support is clearly important and social services should be involved early to advise regarding long-term care, respite and financial benefits. There is a Department of Health funded National Care Package based at the National CJD Surveillance Unit in Edinburgh that provides advice and support including funding for necessary additional equipment. The National Prion Clinic in London also acts in an advisory capacity.

Diagnosis of CJD often takes some time, due to the rarity of the condition and the lack of a definitive, non-invasive test. This can be a very distressing period for the family, particularly as they see their loved one deteriorate in front of their eyes. Various support groups are available including the CJD Support Network (affiliated to the Alzheimer's society) and the Human BSE Foundation (run by relatives of sufferers of variant CJD).

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The views expressed in this factsheet are those of the author, not necessarily those of the NWDC.

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