What is Creutzfeldt-Jakob Disease (CJD)?

CJD is a rare and fatal degenerative brain disease in humans. CJD is one of a group of diseases that affects humans and animals known as transmissible spongiform encephalopathies (TSE) or prion disease. In animals the best known TSE is BSE (bovine spongiform encephalopathy) commonly referred to be the media as 'mad-cow' disease.

Classical CJD (cCJD)
For simplicity, the term 'Classical CJD' is used in the National Infection Control Guidelines to describe all forms of human CJD except Variant CJD (vCJD). Variant CJD, also commonly known as 'Mad Cow' Disease is related to the consumption of BSE contaminated beef and to date we have had no reported cases of vCJD in Australia.

In Australia we average about 25 – 35 cases of classical CJD a year. Symptoms of CJD include lose of memory, dementia, confusion, patients often become clumsy and lack coordination which is known as ataxia and can develop jerking movements known as myoclonis. The rapid decline, particularly with sporadic CJD is very characteristic.

Classical CJD includes

- Sporadic CJD (sCJD)
- Genetic or inherited CJD (gCJD)
- Iatrogenic or medically acquired CJD (iCJD)

Sporadic CJD is a rapidly progressive disease that has no known cause. It occurs at random in about one person per million of population per year and accounts for 85% – 90% of all cases of prion disease. sCJD mainly affects people in the 50 – 70 year age group The length of illness can vary but sporadic CJD is often recognised for the rapid progression with survival usually only 3 – 6 months.

CJD is unique in that is can be genetic and is transmissible.

Genetic CJD accounts for only between 5% and 15% of cases of classical CJD. Genetic CJD includes the following:

- Familial CJD (fCJD)
- Gerstmann-Straussler Scheinker Syndrome (GSS)
- Fatal Familial Insomnia (FFI)

Genetic CJD is usually recognised from a family history of the illness in two or more blood relatives or can be diagnosed from a positive prion protein gene (PRNP) on the patient. In genetic CJD there is a defect in the gene encoding of the prion protein and it is inherited in families in an autosomal dominant fashion from generation to generation at a rate of 50%. Each person carrying the genetic mutation has a 50% chance of passing it onto each of their children. For someone carrying the gene they will eventually develop the disease but there is no test to know when or if they will live long enough to actually become symptomatic.

Most forms of familial CJD are impossible to differentiate from sporadic CJD and it is not until a gene test is done that a genetic cause can be established or ruled out. Patients with GSS often survive for several years and patients with FFI suffer from a progressive and untreatable form of insomnia.

An autopsy is the only way to obtain a definite diagnosis of CJD. Once a diagnosis of CJD has been confirmed by autopsy a DNA test on tissue can be done if the family wish to know if there is a genetic cause. This is a separate test that needs to be consented to by the family and genetic services can be helpful in assisting families through the decision process. Alternatively, testing can be done on a blood sample taken from the patient with suspected CJD if there is evidence of a family history of genetic CJD or possibly if the family have strong reasons not to consent to an autopsy.

CJD is transmissible and it was in the 1960's that it was realised that Kuru, a prion disease affecting the Fore people of Papua New Guinea, was transmitted through cannibalism.

Iatrogenic CJD is the form associated with medical treatments. Although rare, iatrogenic CJD has occurred due to the use of human derived pituitary hormones for fertility and short statue, dura mater grafts and corneal transplants. There is also a recognised risk of transmission from the use of contaminated instruments used in procedures involving high infectivity tissues such as brain, spinal cord and posterior of the eye.

Variant CJD was first recognised in 1996 following the first death in 1994 in the UK. There have been over 200 cases, mainly in the UK, as a result of the consumption of BSE contaminated products and it is now known that vCJD can be transmitted through blood and blood products. Variant CJD is clinically quite different to classical CJD and looks more like Kuru, has a longer duration of illness, presents often with psychiatric symptoms and affects a much younger age group (average age 27 years). Abnormal forms of the prion protein are often found in peripheral tissues such the spleen, lymph nodes and tonsils which pose extra risks of transmission that does not occur in classical CJD.

From the Kuru experience in Papua New Guinea we have also learnt that incubation periods can be as long as 50 years and this may be dependant on our genetic makeup. There are two different types of amino acid – methionine (M) or valine (V). As everyone has two copies of the gene, they can be MM, MV or VV, with 47% of the population being MV. Almost all of the patients with vCJD have been MM which researchers indicate may influence the incubation period. The incidence of vCJD is declining but there is fear that there may be another wave of vCJD amongst VV and MV genetic type people.

Why does this disease have such an impact on the blood supplies in Australia and attract screening questionnaires on admission forms in many hospitals in Australia?

Although there is no proof that classical CJD can be transmitted by blood there is also no proof that it cannot and for those who are at increased risk of developing CJD in Australia, for example over 2000 people who were on the human pituitary program up until 1985 and people who have received dura mater grafts during neuro-surgery until 1989, there is no way of knowing if they are incubating CJD. As the years pass we are more confident that there will not be any further cases relating to these medical procedures but with the research available and the lessons we have learnt from Kuru it is impossible to say and people who have been identified as having an increased risk of developing CJD, will continue to be deferred from donating blood and face screening questionnaires on CJD on admission form in hospitals and other facilities.

For family members, where genetic CJD has not been ruled out by predictive testing on the individual, they are assumed to be at risk by the Australian Blood bank as a precaution only but if genetic CJD in the family has been ruled out by genetic testing on the index patient then family members, although still deferred from donating blood, there should not be any requirement for special precautions for any medical procedures.

For individuals 'at increased risk of CJD' following a contamination incident, genetic family members, and family members where a genetic cause has not been ruled out, the national infection control guidelines recommend special precautions be followed for instruments used on these patients but only when surgery involves high infectivity tissue such as brain, spine and posterior of the eye.

Disclosure of risk is a moral obligation and not a legal obligation so it is important when people disclose their 'at risk of CJD' status that they are not discriminated against as this causes a real reluctance to disclose in the future.

Note: An individual from a known genetic family who themselves has had a negative result to a prion protein gene (*PRNP)* test will be accepted as a blood donor by the Australian Red Cross Blood Service.

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