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Creutfeldt-Jakob – draft policy December 2016

Creutzfeldt-Jakob disease (CJD) is a devastating illness that is universally fatal. There is no treatment that can delay or prevent death. Because CJD is rare, many health professionals dealing with a patient with suspected CJD have never seen a case before.

Contents:

1. Background

CJD is a rare, rapidly progressive dementing illness that occurs in about 1- 2 patients per million per year worldwide. CJD belongs to a group of rare diseases known to affect humans and animals called transmissible spongiform encephalopathies (TSE) or prion disease. The transmissible agent is known as a prion which is primarily composed of protein

Classification

Sporadic CJD
Around 90% of patients with CJD in Australia have sporadic CJD (sCJD) which has no known cause and there is no effective treatment. sCJD mainly affects people aged 50-85 (93%) and the length of illness can vary. However, sporadic CJD often progresses quickly with survival of only 3-6 months.

Familial CJD and Iatrogenic CJD
The remaining approximately 10% have genetic forms of prion disease, or develop the disease as a late complication of transmission from prior treatment with human derived pituitary hormone treatment, corneal transplants or dura mater grafts. This second form is referred to as medically acquired or iatrogenic CJD (iCJD). The number of iCJD cases has declined dramatically in recent years.

Variant CJD
Variant CJD (vCJD) usually occurs in younger patients. It is associated with the consumption of contaminated beef from cattle exposed to products infected with the prion protein that causes bovine spongiform encephalopathy (BSE). This occurred in the UK during the 1980s and early 1990s and the first case of vCJD was described in 1996. It became commonly known as “Mad Cow Disease”. To date there have been 229 cases globally but the majority in the UK. It is important to note that variant CJD has never been identified in Australia. The term “Mad Cow disease” should **not** be used to describe CJD in humans.

The natural history of vCJD is typically quite different from other forms of CJD. It has a longer duration of illness (approximately 14 months), often presents with psychiatric and sensory symptoms and affects a much younger age group (median age of death 28 years). Abnormal forms of the prion protein are often found in peripheral tissues (spleen, lymph nodes, tonsils, blood) and can pose extra risks of transmission that do not occur in other forms of CJD.

2. Clinical features

Onset
Average age at onset of symptoms in CJD is 65 years, and most cases occur between 50 – 75 years. Most patients die within a year, and survival beyond 2 years is very rare.

Symptoms
Rapidly progressive mental deterioration and myoclonus are the two cardinal clinical manifestations of sCJD.

- **Mental deterioration** may manifest as dementia, behavioural abnormalities, or deficits involving higher cortical function. Changes in concentration, memory, and judgment are frequent early signs.
- **Mood changes** such as apathy and depression are common. Euphoria, emotional lability, and anxiety may also occur but frequently.
- **Sleep disturbances**, particularly hypersomnia, but also insomnia, are also common, and may be a presenting sign.
- **Myoclonus**, especially provoked by startle, is present in more than 90% of patients at some point during the illness but may be absent at presentation, even when dementia is profound.
- **Extrapyramidal signs** such as hypokinesia and **cerebellar manifestations**, including nystagmus and ataxia, occur in approximately two-thirds of patients and are the presenting symptoms in 20- 40%.
- **Signs of corticospinal tract involvement** develop in 40- 80% of patients. Signs include hyperreflexia, extensor plantar responses (Babinski sign), and spasticity.

Progression
As CJD progresses, dementia becomes dominant in most patients and can advance rapidly.

Eventually the patient will lose the ability to move and speak (akinetic mutism).

3. Diagnosis

The gold standard for diagnosis of CJD is a neuropathological examination of the brain (usually performed post-mortem).

The main histologic features of prion disease are

- Spongiform change
- Neuronal loss (particularly of cortical layers III-V) without inflammation
- Accumulation of the abnormal prion protein

Families are not obliged to consent to a post mortem.

The diagnosis of presumed CJD is based on the clinical features of:

- Rapidly progressive dementia, and
- At least two out of the following four clinical features: myoclonus; visual or cerebellar disturbance; pyramidal/extrapyramidal dysfunction; akinetic mutism
- Positive 14-3-3 result in CSF, diagnostic MRI or diagnostic EEG.
- Absence of a more likely alternative diagnosis

The diagnosis should be made by a Neurologist.

4. Family support and care of the patient

The presenting symptoms, rapid decline and uncertainty in diagnosis as well as lack of effective treatment for CJD mean that patients and families require considerable support. They will often know very little about CJD except the misconception that it is "mad cow disease". Googling often incites fear regarding transmission and genetic risk and once a patient is classified as 'suspected CJD' there is often a feeling of stigma. The family are then asked to consent to an autopsy for diagnosis.

It is important to offer support and counselling to the family early, and the parent unit (usually Neurology) **should involve Palliative Care as soon as the diagnosis has been made**. A family meeting is recommended to allow the patient (if appropriate) and family to discuss the diagnosis, prognosis and care planning with the team. The meeting should be multidisciplinary and involve the parent medical unit, palliative care, nursing and allied health including social work as a minimum. Pastoral care teams are invaluable in supporting the family in both managing the stigma and rapid decline of their loved one**.**

Families should be offered referral to the CJD Support Group Network as soon as the diagnosis is suspected. They can help families navigate the difficult issues of autopsy, diagnostic and genetic testing, and consent. The Palliative Care service has information booklets from the CJD Support Group Network.

Care planning should involve explanation of symptoms, deterioration and care requirements. The following aspects of care should all be discussed:

- **Psychotic symptoms** are particularly frightening for patients and families. Education is required for family regarding this. Second generation anti-psychotics may moderate, but not eradicate, these symptoms.
- **Heightened sensitivity to touch, light and noise.** A single room is recommended. Avoid sudden movements, use quiet voices and provide consistency of caregivers.
- **Myoclonus** is quite distressing for observers but less so for the patient. Benzodiazepines such as clonazepam may be helpful.
- **Anxiety, restlessness** benzodiazepines such as clonazepam can be helpful.
- **Resistance to care is** very distressing for family members. There is a role for benzodiazepines, in particular clonazepam, in management of agitation, myoclonus and seizures.
- **Seizures may occur**. They can be treated with benzodiazepines such as clonazepam.
- **Pyrexia "greasy sweat"** is a feature of disease and may not represent superimposed infection.
- **Urinary and faecal retention**, and later incontinence. This may be managed with a urinary catheter and a bowel regime.
- **Dysphagia and aspiration**. Discussion regarding feeding and patient's eventual inability to sustain adequate hydration or nutrition. Discussion around the role of artificial hydration and nutrition, and how it can potentially be more problematic for the patient.

The CJD Support Group Network has also published a detailed handbook for health professionals describing presentation, diagnosis, frequently asked questions, and care of the patient and family, before and after death. An information package, including the handbook and a DVD 'Understanding CJD', is available by calling 1800 052466 or emailing contactus@cjdsupport.org.au

5. Important issues that must be discussed with families before death

Two main issues need to be discussed with relatives early, so that arrangements can be made before the patient's death.

a. Autopsy

This is highly recommended for patients who have died from suspected CJD to confirm the diagnosis.
From a public health point of view, it is very important to identify variant CJD vs other forms. However, whilst the autopsy *can* differentiate variant CJD from other forms, it cannot differentiate familial CJD from sporadic cases. The family can choose to consent to a DNA test to investigate for possible familial CJD.

Furthermore from the family's perspective, there are lifelong implications if they have a relative who has died of suspected CJD. First and second degree relatives are unable to donate blood (although this policy may be revised later in 2016 if the DNA test rules out a genetic cause). Organ donation may also be restricted, and they may require special precautions for elective surgery.
A list of frequently asked questions about autopsy is in Appendix B. This is important to read before discussing the process with patients and their families.

The Palliative Care Service can assist in this process, and it is recommended that families are offered referral to the CJD Support Group Network. Autopsies are carried out at the Alfred Hospital.

b. Genetic testing

Familial CJD may be suspected when there are two or more affected first degree blood relatives. Familial CJD is rare and confirmation requires the identification of a mutation within the *prion protein gene* (PRNP) in a symptomatic individual. Analysis of the PRNP gene can be performed on patient DNA, either from a blood or tissue sample.

Typically familial CJD is inherited in an autosomal dominant fashion (i.e the child of the index patient with familial CJD has a 50% chance of inheriting the genetic change within the PRNP gene). However, the mutation has variable penetrance, which means that all individuals with a given genetic change will not necessarily follow the same clinical course. Whilst individuals who inherit the familial mutation will most likely develop the illness in their lifetime, there is no test to predict the likely age of symptom onset or rate of cognitive decline.

For example, one sibling with the familial mutation may present aged 20 while another may remain unaffected at 75.

There are 2 options in regards to genetic testing for familial CJD.

1. **Premortem** blood sampling- (see appendix D for description of procedure). Enables earlier diagnosis or storage of blood/DNA samples for testing at a later stage. This method is preferred. PRNP sequencing may be requested whilst the patient is still living if clinical suspicion is high. Alternatively families may consent for DNA to be stored from a blood sample with specific testing carried out once a post-mortem has confirmed the clinical diagnosis. In both cases, informed consent must be obtained from the next of kin/ MEPOA prior to initiating genetic testing as the implications for extended family are significant.
2. **Postmortem** tissue (brain) sample. Once a diagnosis has been confirmed by neuropathological examination, DNA can be extracted from autopsy tissue by the ANCJDR and made available for genetic testing. DNA extraction from autopsy tissue is a fee-based service.

Consultation with a specialist clinician and a clinical genetics service (specifically the Victorian Clinical Genetics Services) is recommended to ensure that the requesting individual/family fully understand/s the test procedure, benefits, limitations and the possible consequence of the test result

6. Requirements for doctors

a. Notify Victorian Department of Health

CJD is a notifiable disease. It is a Group B condition that requires **WRITTEN** notification within five days of initial presumed diagnosis.
The forms and online notification are available from the Department of Health website: www.health.vic.gov.au/ideas, or via the link on the Austin intranet Infectious Diseases page.

b. **Report suspected case to the Australian National CJD Registry** (details in Appendix A). This is for epidemiological and autopsy purposes. They are a good resource and may be helpful at guiding doctors through the necessary processes as CJD patients reach the terminal phase.

c. **Complete the following forms**, following informed consent discussion by the Registrar or Consultant with the patient's Enduring Medical Power of Attorney, or senior NOK

- Autopsy consent form (contact Austin Health Anatomical Pathology for copy) if the family has decided to proceed with an autopsy. This should be completed by a registrar or consultant.
- NOK consent release form for the ANCJDR (provided by ANCJDR) if family are agreeable to be contacted.

d. **Contact the Alfred Hospital pathology department** (Appendix A) when the patient is in the terminal phase of their illness and death is expected. Let them know that CJD is suspected or confirmed and that you will need a CJD autopsy.

e. **Ask the family to nominate a funeral director**.

f. **Notify the nominated funeral director that a limited, brain only autopsy is taking place on the patient.** (If the family has decided to proceed with autopsy).

g. **Ensure the completed death certificate and the signed autopsy consent form accompanies the body of the patient to the Alfred Hospital** for an autopsy to proceed. This is not a coroner's autopsy and the treating team can complete the death certificate.

h. **Conduct the public health screening questionnaire with the patient's NOK** and email completed questionnaire back to the ANCJDR (ancjd-reg@unimelb.edu.au):
- Blood donation history in last 3 years prior to onset
- Surgical history last 2 years prior to onset
- History of organ donation or receipt
- Travel history to the UK (1980-1996)
- Family history of human prion disease (CJD or other neurodegenerative illness)
- Hormone recipient history (hPG/hGH treatment – up to 1988)

7. Nursing care after death

Standard universal infection control precautions apply for the care of a patient with suspected CJD.
CJD is transmissible from one person to another **only** through invasive medical procedures involving the central nervous system via transfer of the contaminated prion protein.
Nursing a CJD patient or kissing a loved one with CJD does not pose any risk of transmission.

8. Authors:

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