Creutzfeldt-Jakob disease surveillance in Australia January 1970 to December 2003

Genevieve M Klug,[1] Victoria Lewis,[1] Alison Boyd,[2] James S Lee,[1] Colin L Masters,[3] Steven J Collins[3]

Abstract

The Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) was established by the Commonwealth Government in October 1993 in response to the recognition of four probable human pituitary hormone related Creutzfeldt-Jakob disease (CJD) deaths. An inquiry[1] into CJD in Australia and the use of human pituitary hormones under the Australian Human Pituitary Hormone Program suggested the expansion of some activities of the Registry to include retrospective case ascertainment from 1 January 1970. In parallel with monitoring possible medically acquired (iatrogenic) cases of CJD, the ANCJDR prospectively monitors and investigates all suspect cases of transmissible spongiform encephalopathies occurring within the states and territories of Australia, including sporadic and familial, and the potential occurrence of variant CJD. The ANCJDR also actively participates in an international surveillance consortium. This brief report summarises methods of classification and ascertainment as well as current epidemiological findings and new surveillance techniques that are being adopted to improve case ascertainment. *Commun Dis Intell* 2004;28;356–358.

Key words: Creutzfeldt-Jakob disease, transmissible spongiform encephalopathies, surveillance

Introduction

Transmissible spongiform encephalopathies (TSE) comprise a group of rare neurodegenerative disorders that are invariably fatal and develop in both animals and humans. Creutzfeldt-Jakob disease (CJD) is the most common human TSE and occurs sporadically, secondary to prion protein gene (*PRNP*) mutations or through medical interventions using contaminated therapeutics/equipment. Variant CJD (vCJD) is zoonotically linked to bovine spongiform encephalopathy (BSE), the commercial bovine livestock form of prion disease, of which Australia remains free as of December 2003.[2,3]

Classification and notification methods

The Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) utilises internationally recognised case definitions for classification of definite, probable or possible cases.[4,5] An incomplete status is given to suspect cases where investigation is pending. Definite cases are those that have been confirmed neuropathologically. Probable cases are classified on the basis of clinical profile and a characteristic electroencephalogram (EEG) and/or a positive 14-3-3 cerebrospinal fluid (CSF) test. Possible cases fulfil the same clinical profile in the absence of an EEG or with an atypical EEG and either no 14-3-3 CSF test or a negative result. The method of classification of possible cases is in accordance with the EUROCJD diagnostic criteria and has been adopted since 1 January 2001.

Case ascertainment relies on the notification of suspect cases to the registry by numerous methods. The most numerically important method for ascertaining cases overall has been personal communication from medical practitioners (41.6% of registry cases). Previous sources of suspect cases include hospital and health department records searches, death certificates searches, communication from the Pituitary Hormone Taskforce, the CJD counselling service and families. Since 1997, requests to the ANCJDR for diagnostic testing by assessing the presence of

1. Research Assistant, Australian National Creutzfeldt-Jakob Disease Registry, Melbourne, Victoria
2. Registry Co-ordinator, Australian National Creutzfeldt-Jakob Disease Registry, Melbourne, Victoria
3. Co-Director, Australian National Creutzfeldt-Jakob Disease Registry, Melbourne, Victoria

Corresponding author: Associate Professor Steven Collins, Australian National Creutzfeldt-Jakob Disease Registry, Department of Pathology, The University of Melbourne, Melbourne VIC 3010. Telephone: +61 3 8344 1945. Facsimile: +61 3 9349 5105. Email: stevenjc@unimelb.edu.au

the CSF 14-3-3 protein has led to an increase in the notification of suspect cases, accounting overall for 19.9 per cent of all registry cases. At present, this source is the most important ongoing mechanism for referral of cases.

Surveillance summary to 31 December 2003

As of 31 December 2003, there were 519 cases on the register with 274 definite cases and 180 probable cases (Table). There were six cases of possible CJD of which five were of sporadic and one iatrogenic. A total of 59 cases were incomplete with 27 of these cases still alive. Four hundred and nine suspect cases have been excluded after detailed follow-up. As of December 2003, no further cases of iatrogenic CJD have been detected since 2000 and Australia remains free of vCJD.

There has been a steady increase in the annual incidence of spongiform encephalopathies since 1970, with rates stabilising in the last few years (Figures 1 and 2). This is consistent with, and analogous to, the experience of other CJD surveillance programs, with the increase probably reflecting case ascertainment bias stemming from improved recognition, reporting, investigation and case confirmation. The average annual age-adjusted mortality rate during the period from 1970 to 2003 is 0.83 deaths per million per year. During the prospective period of ANCJDR surveillance from 1993 to 2003, the average annual rate of mortality was 1.19 deaths per million population. This epoch is considered a more reliable period for analysis because prospective ascertainment was employed, and standardised approaches to case classification and ascertainment were implemented nationally.

Figure 1. Definite and probable cases of Creutzfeldt-Jakob disease on the Australian National Creutzfeldt-Jakob Disease Registry, 1 January 1970 to 31 December 2003

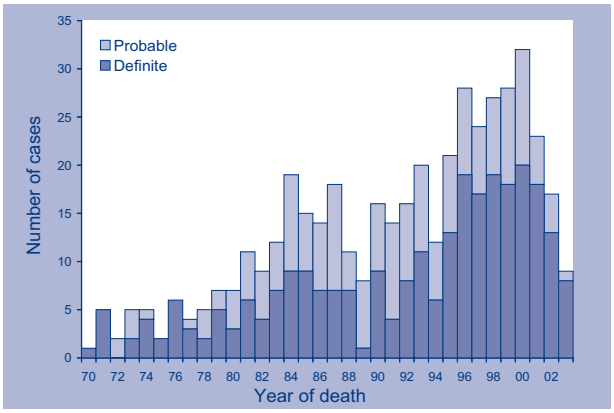
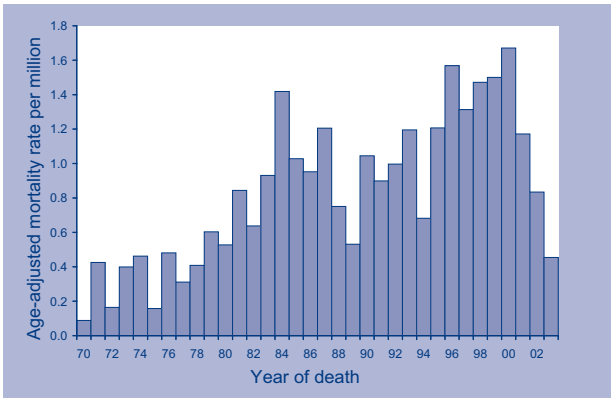


Figure 2. Age-adjusted mortality rates* of definite and probable cases of Creutzfeldt-Jakob disease, 1 January 1970 to 31 December 2003



* Mortality rates were calculated using the Australian Bureau of Statistics 2000 resident population estimates for Australia.

Table. Classification of cases on the Australian National Creutzfeldt-Jakob Disease Registry, 1 January 1970 to 31 December 2003

Classification	Sporadic	Familial	Iatrogenic	Variant CJD	Unclassified	Total
Definite	244	25	5*	0	0	274
Probable	168	8	4	0	0	180
Possible	5	0	1	0	0	6
Incomplete	0	0	0	0	59†	59
Total	417	33	10	0	59	519

* Includes 1 definite iatrogenic case who received pituitary hormone treatment in Australia but disease onset and death occurred while a resident overseas. This case is not included in statistical analysis since morbidity and mortality did not occur within Australia.

† Includes 27 living cases.

The majority of Australian definite and probable CJD cases are sporadic (90.9%). Familial and iatrogenic cases constitute 7.3 per cent and 1.8 per cent, respectively, of all definite and probable cases. The percentage of familial cases observed in Australia is less than the 12–14 per cent reported by European surveillance programs.[6] An explanation for this difference most likely relates to the non-systematic approach to *PRNP* testing adopted in Australia, which from 1997 to 2002 was undertaken in 31 per cent of all definite and probable cases.

The duration of illness for CJD cases varies depending on aetiology. The median length of illness duration for all CJD cases was four months. For sporadic cases, median duration was found to be four months (range, 0.9–60 months), for iatrogenic cases 6.25 months (range, 2–25 months) and for familial cases seven months (range, 1.5–192 months). Familial CJD was found to be associated with a significantly greater survival time in comparison to sporadic CJD ($p<0.0001$ by log rank test).

In sporadic CJD, no significant gender differences have been observed. Overall, 47.6 per cent of cases were male and 52.4 per cent were female. The average age of death in sporadic cases by gender was 65 years (range, 25–88) for males and 67 years (range, 33–89) for females. Over the period 1970 to 2003, there was no difference between the average age-specific mortality rates of males (0.75 deaths/million/year) and females (0.77 deaths/million/year). In males, the peak mortality rate occurred between 70–74 years (4.0 deaths/million/year) and in females between 65–69 years (4.5 deaths/million/year).

In comparison to sporadic cases, the average death age of familial cases was 52 years (range, 20–82 years) in males and 61 years (range, 42–82 years) in females. Peak mortality rates occurred in the 65–69 year age group in both males (0.27 deaths/million/year) and females (0.35 deaths/million/year) and in iatrogenic cases, the average death age was 45 years (range, 27–62 years) for males and 39 (range, 26–50 years) for females.

Analysis of the occurrence of sporadic cases by state of residence showed that the rate of death was not significantly different in any state or territory compared to the rate in the Australian general population. Furthermore, sporadic CJD does not exhibit a significant association with region of birth or travel history of Australian-born cases.

In order to facilitate optimal surveillance, the Communicable Diseases Network Australia agreed to designate TSEs as a notifiable disease. At the time of writing, CJD was notifiable in Tasmania, Victoria, Western Australia and New South Wales with the remaining states and territories to follow.

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