Surveillance of Creutzfeldt-Jakob disease in Australia: update to December 2010

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Abstract

Since the establishment of the Australian National Creutzfeldt-Jakob disease Registry (ANCJDR) its activities have expanded from prospectively investigating additional iatrogenic Creutzfeldt-Jakob disease cases to include: retrospective ascertainment to 1970; provision of expert opinions in the area of infection control management; provide diagnostic testing services for all suspect cases; and maintenance of national and international collaborations in conjunction with routine surveillance responsibilities. An update of the ANCJDR's surveillance activities and outcomes between 1 April and 31 December 2010 is herein presented, including a summation of a recent publication by the ANCJDR. The shorter reporting period is due to a contractual change with the Department of Health and Ageing in 2010, resulting in the reporting timeframe shifting to align with full calendar years. *Commun Dis Intell* 2011;35(2):149–153.

Introduction

In October 1993, the Australian Government Department of Health and Ageing established the Australian National Creutzfeldt-Jakob disease Registry (ANCJDR) and have since charged this unit with the task of the surveillance of human prion diseases in Australia. The formation of this unit was underscored by the recommendations of the Allars Report,[1] which investigated the identification of 4 women who were recipients of human-derived pituitary hormones and who died of Creutzfeldt-Jakob disease (CJD) between 1988 and 1991. CJD is one form of the prion group of neurological disorders, which in humans, includes Gerstmann Sträussler-Sheinker syndrome, fatal familial insomnia, Kuru and variant CJD (vCJD) while bovine spongiform encephalopathy (BSE) in cattle, scrapie in sheep and chronic wasting disease in deer and elk represent principal animal forms of disease. This family of disorders, also known as transmissible spongiform encephalopathies (TSEs), causes a rapidly progressive neurological illness, ultimately leading to death. Globally, the annual incidence of CJD is around 1 case per million, although it is speculated that this may well be higher as has been indicated from several international surveillance centres,[2] where the annual incidence of 2 cases per million per year has been observed. The large majority of CJD cases have no known underlying cause and are thus classified as sporadic. The remaining cases are attributed to iatrogenic transmission or genetic predisposition. All suspect TSE cases referred to the ANCJDR are actively investigated and where possible, classified as definite, probable or possible according to the internationally recognised and validated clinical and neuropathological criteria.[3,4]

ANCJDR surveillance update to 31 December 2010

Notifications

Between 1 April and 31 December 2010 46 new suspect cases of CJD were notified to the ANCJDR. While this figure is reduced from previous reports based on 12 month periods, it is a reflection of the shorter reporting period of 9 months due to a change in contractual timeframes. Of these new suspect cases, nine have been confirmed as definite or probable cases, one has been classified as a possible case and three have been removed from the register. The remaining 33 are still under investigation with 16 of these cases still alive and 17 deceased. Neuropathological examination for nine of the deceased cases is pending.

Since establishment, a total of 1,468 cases of suspect CJD have been notified to the ANCJDR, comprising 308 notifications of case deaths prior to 1993 (retrospective cases) and 1,160 suspects notified prospectively. While this equates to around 80 notifications annually, the notification of prospective cases provides a more accurate estimate of annual national notifications. The average number of suspect case notifications for the period 1993 to 2010 is 64 cases per year or 3.2 cases per million population per year. This is almost 3 times greater than the rate of Australian confirmed cases for the same period (1.2 cases per million per year). Almost half of the prospective notifications stem from referrals for cerebrospinal fluid (CSF) 14-3-3 protein analysis (one of the diagnostic tests offered by the ANCJDR since 1997), while around a third are derived from personal communication from clinicians, family or hospitals. The remaining cases are ascertained through death certificate searches, hospital and health department searches and requests for other diagnostic services such as genetic testing.

By state and territory, analysis of the prospective suspect case notifications shows relatively stable levels since 2006 compared with previous years (Figure 1).

Prior to this report however, Tasmania was an exception to stable notification levels due to declining notifications since 2006. In 2010, 3 cases have been notified to the ANCJDR, returning the number of notifications to expected levels. A reduced number of notifications in New South Wales for 2008–2009 has been sustained in 2010, with around 10 fewer cases being notified for these 3 years compared with the 2006–2007 period.

Case outcomes

Of the 1,468 cases notified to the ANCJDR, 653 of these have been classified as probable or definite CJD cases (Table 1). An additional case of definite iatrogenic CJD is included in Table 1, due to pituitary hormone treatment occurring within Australia. However, due to the non-domestic location of onset and death, this case is not included in the Australian statistical analyses. The remaining, notified cases have been excluded after detailed follow-up investigation (573); are currently under evaluation (229); or have been classified as possible cases (13). Possible cases, classified as clinically likely but unable to meet diagnostic criteria, are excluded from all statistical analyses in this report.

Since the last reporting period, 14 suspect cases have been removed from the register, with 11 of these after neuropathological confirmation. A further definite CJD case, who was initially referred to the register during treatment in Australia, died overseas and was therefore removed from the register and not included as an Australian case due to the non-domestic location at death. For the 9-month reporting period, 20 cases were confirmed as definite cases and four

Figure 1: Prospective, suspect Creutzfeldt-Jakob disease case notifications to the Australian National Creutzfeldt-Jakob Disease Registry, 1997 to 2010, by state or territory

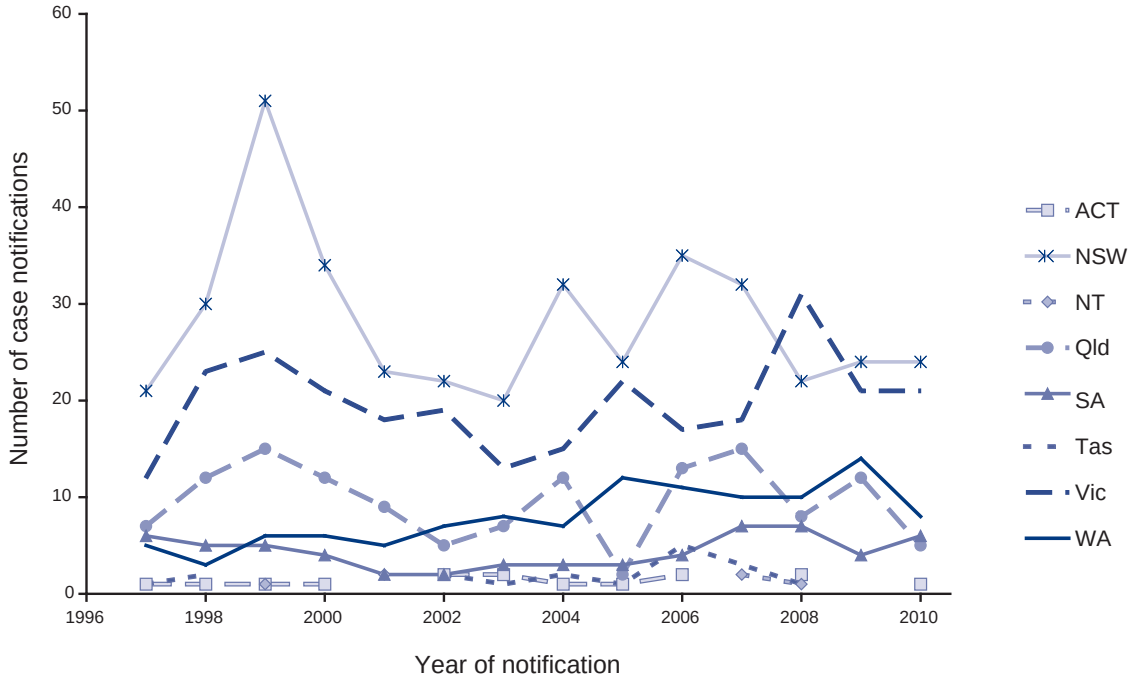


Table 1: Classification of cases by the ANCJDR, 1 January 1970 to 31 December 2010

Classification	Sporadic	Familial	Iatrogenic	Variant CJD	Unclassified	Total
Definite	385	43	5*	0	0	433
Probable	207	10	4	0	0	221
Possible	12	0	1	0	0	13
Incomplete	0	0	0	0	229†	229
Total	604	53	10	0	229	896

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

† Includes 159 living cases.

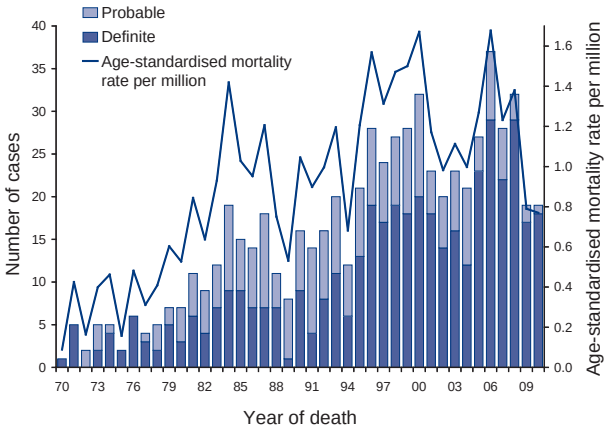
confirmed as probable cases, which is consistent with the number of cases classified in previous full 12 month reporting periods. This finding stems from the greater number of definite cases confirmed after post-mortem examinations performed in 2010 and relates to the reduced turnaround time for post-mortem examinations across some states and territories within this 9-month period, translating into more cases being confirmed in a shorter period of time. Of the new cases, 23 were classified as sporadic cases and one as a familial case.

The annual proportion of suspect cases notified to the ANCJDR where death is known to have occurred and have undergone post-mortem examination, has increased over time. This is to be expected given the active approach that the ANCJDR has undertaken to seek and facilitate post-mortem examinations in recent years. For the 1993 to 2010 period, 60% of all suspect case deaths have undergone post-mortem. It should be noted that this proportion is related only to cases where death is known to have occurred and the ANCJDR is aware that not all deaths are notified. In Victoria, further assistance with post-mortems has been provided through the formalisation of a contractual agreement with the Victorian Department of Health and the ANCJDR. The agreement has led to more expeditious and higher rates of autopsy in this state.

Based on the Australian population, the average crude rate of CJD-related post-mortems between 1993 and 2010 is 1.4 post-mortems per million per year, which is considerable given CJD is a particularly rare condition. By state and territory, the rate ranges from 0.8 CJD post-mortems performed annually per million in Tasmania to 1.5 in both Victoria and New South Wales. Despite the smaller populations in the Tasmania, the Northern Territory and the Australian Capital Territory, the post-mortem rates are all relatively consistent with more populous states and provide a level of confidence that suspect case deaths in these states and territories have a similar likelihood of undergoing post-mortem examination.

As reported previously, the annual incidence of CJD has steadily increased from 1970 to peak in 2000, 2006 and 2008 (Figure 2) with 1.4–1.6 cases per million per year being recorded, equating to 32 to 37 cases per year. For the overall period of 1993 to 2010, an average of 24.5 CJD cases per year are confirmed in Australia and the average age-standardised mortality rate is 1.2 cases per million per year. Although these long term averages align closely with rates observed in other countries with similar surveillance mechanisms in place,[2] it is believed that the incidence in the peak years, more closely reflects the true incidence of CJD in Australia. The ANCJDR therefore aims to achieve this level of case ascertainment.

Figure 2: ANCJDR definite and probable cases 1970 to 2010,* number and age-standardised mortality rate



Age-standardised mortality rates were calculated using the Australian Bureau of Statistics 2000 estimated resident population for Australia.

* To 31 December 2010.

Delineation of the total case deaths by state and territory shows absolute numbers reflecting regional population distributions. The annual number of deaths from definite and probable TSE according to state and territory during 2000–2010 is shown (Table 2). The mean age-standardised rates (1993–2010) indicates that there is little variability between the larger regions of Australia with between 1.0–1.5 deaths per million occurring annually. These rates are in alignment with reported figures from other countries with similar surveillance mechanisms as those in Australia.[5] Furthermore, analysis of sporadic CJD standardised mortality ratios indicate that the rate of death was not found to be significantly different in any state or territory compared with the rate in the Australian general population, indicating that no state or territory had a greater or lower risk of CJD.

The highest TSE (all forms) mortality rates (1993–2010) were observed in Victoria and Western Australia (1.4 and 1.5 deaths per million per year, respectively). Previously, the lowest rates of mortality were observed in the Northern Territory and Tasmania and it was postulated that cases were being under-ascertained in these regions. More recently, an increase in confirmed cases in these less populated states and territories has contributed to the re-alignment of mortality rates to that of the larger states and territories. Tasmania continues to have the lowest TSE mortality in Australia; however, as previously discussed[5] an under-ascertainment of cases prior to 2000 may be responsible for skewing the overall incidence. Furthermore, a confirmed CJD case who was a permanent Tasmanian resident, but died interstate was not attributed to Tasmania due to the non-Tasmanian location at death. It should be noted

Table 2: Transmissible spongiform encephalopathy deaths and mortality rate, by state or territory

State or territory	TSE cases by year of death											Total TSE deaths	Mean age-adjusted mortality rate (deaths/million/year)	
	00	01	02	03	04	05	06	07	08	09	10		00–10*	93–10*
ACT			1		1		1		2		1	6	1.5	1.4
NSW	12	9	7	7	11	10	11	10	5	8	4	94	1.2	1.2
NT							2	1				3	0.9	0.8
Qld	7	3	3	3			7	2	4	3	1	33	0.7	1.0
SA	2			1	2	1	1	3	5	2	2	19	1.0	1.2
Tas			2			1	2					5	0.9	0.6
Vic	9	10	5	9	5	11	9	6	12	4	9	89	1.5	1.4
WA	2	1	2	3	2	4	4	6	4	2	2	32	1.3	1.5
Australia	32	23	20	23	21	27	37	28	32	19	19	281	1.2	1.2

* Includes all deaths occurring between the complete years 1 January 1993 or 1 January 2000 and 31 December 2010.

that the effect of 2 additional confirmed CJD cases in Tasmania would result in the mortality increasing to 0.9 cases per million per year, re-aligning mortality rates more closely to expected levels.

The age group with the highest mortality from all forms of CJD is amongst those aged 65–69 years where 8.3 deaths per million persons occur annually. From the age of 50, incidence increases to peak at 9.0 deaths per million per year in females in the 65–69 year age group and at 7.6 deaths per million per year in males in the 70–74 year age group (Figure 3). After these gender-specific peak age groups, mortality rates decline for both genders, although it should be noted that an increase in the detection of older age cases in recent years has led to a more rounded decline in the age-specific trend in the older age groups. Females are in slight excess (53%) for all forms of CJD, and this is true for familial (55%) and sporadic (53%) groups. In the small number of Australian iatrogenic cases, an equal number of males and females have been affected overall; 3 female pituitary hormone-related cases, 4 male and 1 female dura mater related cases.

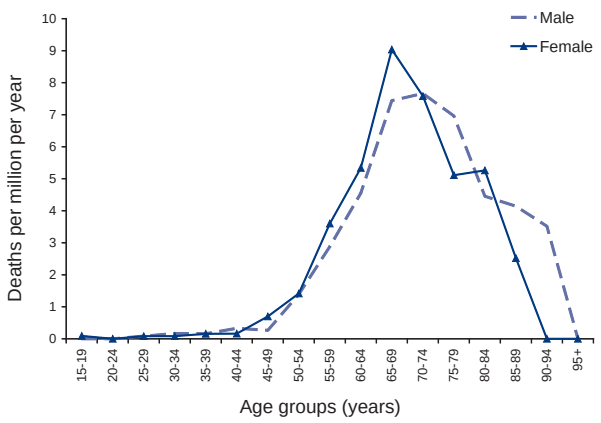
Since the last reporting period, there has been little change in the aetiological proportions of Australian TSE cases with the large majority occurring sporadically (90.7%) and the remainder classified as familial (8.1%) and iatrogenic (1.2%). A slight reduction in the genetic CJD forms has been observed in recent years and while the explanation for this is unclear at present, the incidence of genetic CJD will be closely monitored in future years. There have been no confirmed cases of vCJD, Kuru or further cases of iatrogenic CJD relating to recipients of dura mater grafts or pituitary hormone. The last deaths from iatrogenic CJD occurred in 1991 (pituitary hormone-related CJD) and 2000 (dura mater-related CJD).

As shown in Figure 3, the majority of Australian TSE cases occur after the age of 50 and this is true for all TSE aetiologies. The median age at death in the 653 confirmed cases is 66 years (range, 18–90 years), with the median age younger in familial cases (59 years, range 18–82 years) and iatrogenic cases (39 years, range 26–62 years), but overall closely aligns with the median age death of sporadic cases, given this CJD form represents 90.7% of all cases. Similarly, the median duration of disease from onset to death is 4 months for all cases (range 0.9–192 months) and the sporadic only case group (range 0.9–60 months), yet longer for both the familial case group (6 months, range 1.5–192 months) and the iatrogenic case group (6.5 months, range 2–25 months).

Recent publication

During 2010, the ANCJDR published several articles including an update on pituitary hormone cases in Australia, drawing on the experience in other countries for comparative analysis.[6] In brief,

Figure 3: Age- and sex-specific mortality rates in all Creutzfeldt-Jakob disease cases, 1993 to 2010



this review examined the ongoing risk for individuals who received pituitary hormone extracted from cadavers between 1967 to mid-1985 for the treatment of infertility and short stature under the Australian Human Pituitary Hormone Program. This program ceased in mid-1985 after the recognition of a linkage between treatment and CJD in a recipient in the United States of America. Australia had the lowest rate of pituitary hormone-related CJD cases across the countries compared, with the reasons for this not entirely clear. In addition, given 20 years has passed since the last case of pituitary hormone-related CJD was identified in Australia, the review discusses the current risk for the recipient community and raises the potential for changes to the infection control measures for this recipient cohort in the future.

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