Creutzfeldt-Jakob disease: Australian surveillance update to December 2005

Genevieve M Klug, Alison Boyd, Victoria Lewis, Samantha L Douglass, Rebecca Argent, James S Lee, Colin L Masters, Steven J Collins
Australian National Creutzfeldt-Jakob Disease Registry

Abstract

Australia-wide prospective surveillance of human transmissible spongiform encephalopathies (TSEs) has been conducted by the Australian National Creutzfeldt-Jakob Disease Registry (ANCJDR) since October 1993. In addition, the Registry retrospectively ascertained TSE cases within Australia from 1970. Referrals of all suspect cases of human prion diseases or TSEs are investigated by the ANCJDR and include Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker syndrome, fatal familial insomnia and variant CJD. This semi-annual progressive update presents epidemiological findings of the ANCJDR based on Australian data obtained for the period 1970 to 31 December 2005. *Commun Dis Intell* 2006;30:144–147.

Keywords: disease surveillance, Creutzfeldt-Jakob disease, transmissible spongiform encephalopathies

Surveillance summary to 31 December 2005

From 1 October 1993 to 31 December 2005, the ANCJDR has been notified of 1,061 suspect transmissible spongiform encephalopathy (TSE) cases in Australia whose disease onset and death occurred after 1 January 1970. Of these, 447 cases have been excluded as non-TSE cases. Based on the EUROCJD diagnostic criteria,[1] 504 cases have been classified as definite (311) or probable TSE (193) and a further eight cases have been classified as possible (Table 1). The majority of the definite and probable cases are sporadic (90.4%), while the remainder are familial (8%) and iatrogenic cases (1.6%). The eight possible cases have been classified as sporadic (7) and iatrogenic (1). One-hundred and two cases are currently under investigation with 55 of these cases still alive. During 2005, 66 new suspect cases have been evaluated by the ANCJDR. Nine of these cases have been excluded from the register, 44 remain under review, and 13 have been classified as definite cases after neuropathological examination. As of 31 December 2005, no variant CJD cases and no further iatrogenic CJD cases have been identified in Australia.

Table 1. Classification of ANCJDR cases, 1 January 1970 to 31 December 2005

Classification	Sporadic	Familial	Iatrogenic	Variant CJD	Unclassified	Total	Cases classified during 2005*
Definite	275	31	5†	0	0	311	+18
Probable	180	9	4	0	0	193	+7
Possible	7	0	1	0	0	8	+1
Incomplete	0	0	0	0	102‡	102	+16
Total	462	40	10	0	102	614	+42

* Describes the classifications made during the 2005 surveillance year (includes cases notified in 2005 or previous years).

† Includes one 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 55 living cases.

Corresponding author: Miss Genevieve Klug, Australian National Creutzfeldt-Jakob Disease Registry, Department of Pathology, The University of Melbourne, VIC 3010. Telephone: +61 8344 1949. Facsimile: +61 9349 5105. Email: gmjak@unimelb.edu.au

For the prospective ascertainment period of 1993 to 2005, an average of 82 suspect cases per year have been notified to the ANCJDR for investigation. During this period, annual notifications have varied, which may reflect in part the varied ascertainment methods employed by the ANCJDR during particular time periods as previously described[3] (Figure 1). Since 2000, the annual number of notifications has been relatively constant (approximately 60 suspect cases notified per year). A comparison of the notifications by state and territory between 1993 to 2005 shows that the number of notifications has been relatively stable in the larger states, while in more recent years, notifications have slightly declined in several of the states and territories with smaller populations (Figure 1, Table 2).

Figure 1. Notifications of suspect cases to the ANCJDR, 1993 to 2005, by state or territory

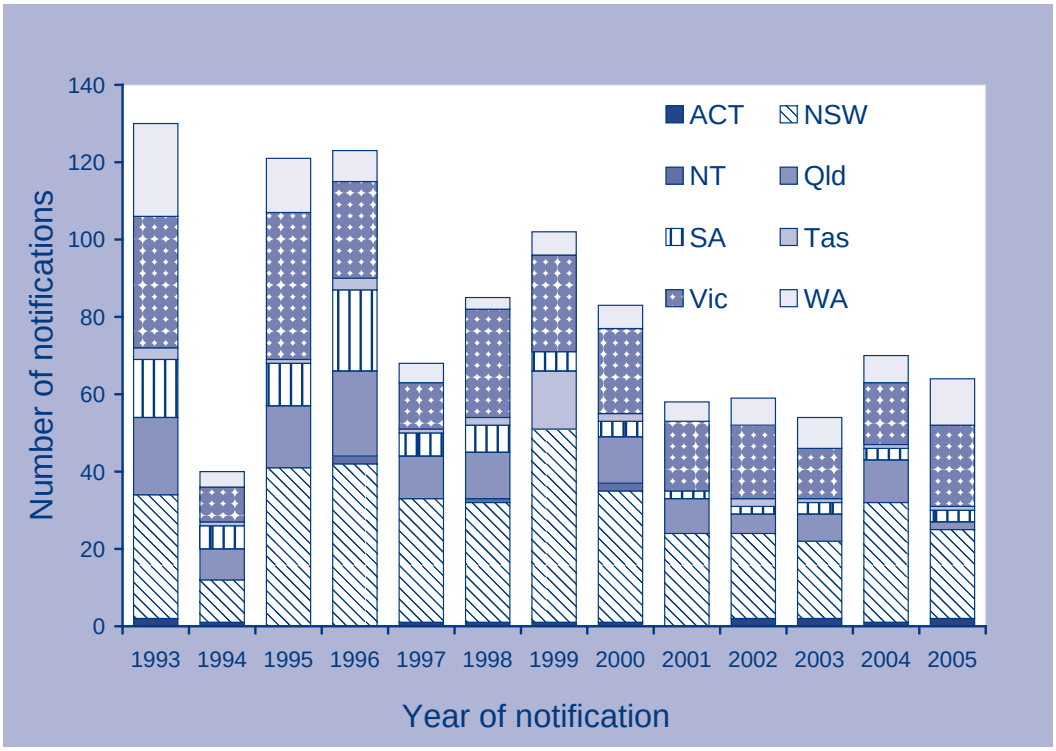


Table 2. Number of suspect cases notified with or without post mortem examinations, 1998 to 2005, by state or territory

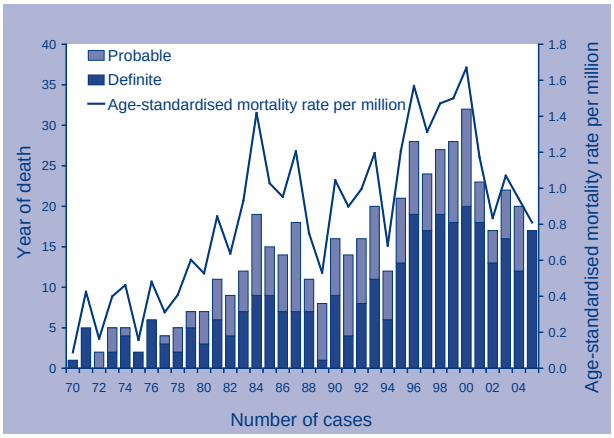
Death year	State or territory of suspect cases*															
	ACT		NSW		NT		Qld		SA		Tas		Vic		WA	
	n	PM	n	PM	n	PM	n	PM	n	PM	n	PM	n	PM	n	PM
1998	1	0	17	8	1	0	4	3	4	3	0		10	6	3	2
1999	1	0	20	11	0		9	6	5	4	0		9	5	1	1
2000	0		21	13	1	0	9	5	2	2	2	0	13	9	5	4
2001	1	0	22	12	0		8	7	2	1	0		13	6	3	1
2002	2	0	17	9	0		5	4	2	2	3	2	15	5	5	3
2003	0		18	13	0		5	2	3	2	0		11	6	8	2
2004	1	0	20	9	0		5	2	2	1	0	1	8	6	2	1
2005	0		17	9	0		1	0	0		1		13	10	6	2
Total	5	0	152	84	2	0	4	29	20	15	6	3	92	0	38	16

* Where death is known to have occurred.

PM Post mortem

A clear increase in the annual incidence of Australian TSEs was observed during the period of 1970 to 2000 (Figure 2). This increase has also been observed in international CJD surveillance units and probably reflects case ascertainment bias associated with heightened recognition and case notification as well as improved investigation and case confirmation.[4] Since 2000, the number of TSE deaths has declined and stabilised at approximately 20 cases per year. In particular, a decline in the number of probable cases has been observed and this probably relates to a number of issues, including broadened surveillance responsibilities and difficulties encountered following changes to privacy legislation. For the period of 1970 to 2005, the average annual age-adjusted mortality rate was 0.85 deaths per million per year. During the prospective period of ANCJDR surveillance from 1993 to 2005, the average annual rate of mortality

Figure 2. Number and age-standardised mortality rate of ANCJDR definite and probable cases, 1970 to 2005



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

was 1.19 deaths per million persons which is similar to the rates reported by other countries undertaking prospective ascertainment.[4]

Of the 455 sporadic cases, 53 per cent were female and 47 per cent were male. This ratio has been consistently observed and suggests no sex predilection. The median age of death is 67 years (females, 68 years; males, 66 years) with a range of 25-89 years. The median illness duration from onset to death of sporadic CJD cases is four months (females, 4 months; males, 3 months); however duration ranges from 0.9 to 60 months. Overall, the 70-74 year age group had the highest mortality rate from sporadic CJD with 4.2 cases per million per annum. In females, the mortality rate peaks in the 65-69 year age group with 4.8 cases per million per annum, whereas in males, the maximum rate is 4.1 cases per million per annum in the 70-74 year age group.

Familial CJD similarly shows no clear sex bias. Of the 40 cases, 55 per cent were female and 45 per cent were male. Typically, the duration of disease and age at death of familial cases is longer and younger respectively, when compared with sporadic CJD.[4] The median duration of Australian familial cases was found to be seven months (range, 1.5-192 months) which is significantly longer than the duration of sporadic CJD cases ($p<0.0001$ by Log Rank Test). Median age at death was 59 years but has been as young as 20 years or as old as 82 years. When comparing male to female cases, death occurred at an earlier age in males (median, 51 years; range, 20-82 years). For females, median age at death was 62.5 years (range, 38-82 years). Mortality rates in familial cases peaked in the 65-69 year age group for both males and females and overall, the rate of death was 0.33 familial cases per million per annum in this age group.

A total of nine iatrogenic cases of CJD have been identified in Australia. These comprise five dura mater graft-related cases (2 definite, 3 probable), three human-derived pituitary gonadotrophin-related cases (2 definite, 1 probable) and one possible human-derived pituitary growth hormone case. One additional case of gonadotrophin-related CJD received treatment in Australia, but disease onset and death occurred while a resident in the United Kingdom and thus is not included in the analysis of Australian cases. Of the dura mater cases, 80 per cent were male and the median age at death was 46.5 years (range, 27-62 years) with median duration 2.5 months (range, 2-10 months). In the remaining female case, death occurred at 26 years after a duration of disease of 3.5 months. In the three female gonadotrophin-related cases, the median death age was 41 years (range, 37-50) and duration was longer than the dura mater-related cases at 10 months (range, 3-25 months). As of 31 December 2005, no further cases of iatrogenic CJD have been detected since the last identified dura mater-related CJD case in 2000.

Analysis of the distribution of CJD cases according to state and territory shows an alignment with the relative population distributions (Table 3). No significant increase in mortality from sporadic CJD has been observed for a particular state or territory when compared to the national rate, indicating no increased or decreased risk. A comparison of the temporal pattern of CJD case numbers and average annual crude incidence for each state or territory between 1993 to 2005 (Table 3) suggests that in a number of states or territories of Australia, there is a decline in the ascertainment of CJD cases in

Table 3. Australian transmissible spongiform encephalopathy (TSE) deaths, 1993 to 2005, by state or territory

State or territory	TSE cases by year of death													Total	Mean crude mortality rate (deaths/million/yr)
	93	94	95	96	97	98	99	00	01	02	03	04	05		
ACT		1					1			1		1		4	0.98
NSW	2	3	7	6	10	10	13	12	9	4	7	11	5	99	1.18
NT						1								1	0.41
Qld	5	2	5	6	3	3	7	7	3	3	3			47	1.05
SA	1	3	2	3	3	1	3	2			1	1		20	1.04
Tas				1						2			1	4	0.65
Vic	10		4	8	5	9	3	9	10	5	8	5	9	86	1.40
WA	2	3	3	4	3	3	1	2	1	2	2	2	2	30	1.27
Total	20	12	21	28	24	27	28	32	23	17	21	20	17	291	1.18

more recent years. In some regions this coincides with lower notifications to the ANCJDR and fewer post-mortems of suspect cases (Table 2). In the more populous states and territories, the number of CJD cases and those suspect cases that are investigated by post-mortem examination have remained constant. Overall, post-mortem examination has been performed on 56 per cent of all Australian CJD cases and 55 per cent of all suspect cases notified to the ANCJDR where death is known to have occurred since 1993.

Since May 2003, six Australian states and territories have included CJD as a notifiable disease. To date, no clear increase of suspect case notifications has been observed. In contrast, notifications to the ANCJDR have slightly decreased in regions where CJD has not been scheduled as a notifiable disease. The ANCJDR will continue to evaluate the influence of compulsory notification on CJD notifications.

Acknowledgements

The ANCJDR wishes to thank families, medical practitioners and associated staff for their generous support of Australian CJD surveillance. The ANCJDR also thanks Dr Handan Wand, Dr Matthew Law and Professor John Kaldor (National Centre in HIV Epidemiology and Clinical Research at the University of New South Wales) for their expert epidemiological and statistical support.

References

1. Will RG. Prion related disorders. J R Coll Physicians Lond 1999;33:311-315.

2. Zerr I, Pocchiari M, Collins S, Brandel JP, de Pedro Cuesta J, Knight RS, *et al.* Analysis of EEG and CSF 14-3-3 proteins as aids to the diagnosis of Creutzfeldt-Jakob disease. *Neurology* 2000;55:811-815.

3. Klug GM, Boyd A, Lewis V, Kvasnicka M, Lee JS, Masters CL, *et al.* Creutzfeldt-Jakob disease: Australian surveillance update to 31 December 2004. *Commun Dis Intell* 2005;29:269-71.

4. Ladogana A, Puopolo M, Croes EA, Budka H, Jarius C, Collins S, *et al.* Mortality from Creutzfeldt-Jakob disease and related disorders in Europe, Australia, and Canada. *Neurology* 2005;64:1586-1591.