

Reappearance of human cases due to Murray Valley encephalitis virus and Kunjin virus in Central Australia after an absence of 26 years

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Abstract

Murray Valley encephalitis (MVE) and Kunjin virus disease are endemic in the tropical parts of the Northern Territory and Western Australia, but have been absent from Central Australia since 1974. In 2000, 5 laboratory-confirmed cases of encephalitis occurred over a short period in the normally dry inland region of Central Australia. The sudden occurrence of cases in March and April 2000 followed unusually high rainfall in the preceding months and evidence of flavivirus activity in the endemic areas in the Kimberley region of Western Australia. Further cases were reported in the following wet season, without preceding human cases in known endemic areas. These findings indicate the reintroduction of these viruses into Central Australia and establishment of local cycles of infection with an ongoing risk to the local population. This area may also act as a potential source for reintroduction of MVE into south-eastern Australia. *Commun Dis Intell* 2002;26:39-44.

Keywords: Murray Valley encephalitis, Kunjin, encephalitis, flavivirus, Central Australia

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Introduction

Murray Valley encephalitis (MVE) and Kunjin (KUN) are mosquito-borne flaviviruses found in Australia.¹ Human infections are usually asymptomatic, though a small percentage develop clinical disease manifesting as febrile illness with headache, as polyarthralgic illness or as encephalitis.^{2,3,4,5} Encephalitis has high mortality and morbidity. Nearly all cases of encephalitis have been due to MVE and relatively uncommonly due to KUN.^{3,5,6} Both viruses are believed to survive in cycles of infection between birds and mosquitoes in enzootic foci in the Kimberley region of Western Australia, the Top End of the Northern Territory and possibly northern Queensland.^{7,8} Spread outside these areas is thought to occur when flooding allows migration of infected waterbirds that introduce the virus into local populations. This is thought to be the mechanism for epidemic disease in areas of Western Australia south of the Kimberley, south of the Top End in the Northern Territory and for the rare occasions of spread into south-eastern Australia.^{1,7,9,10,17}

Culex annulirostris is the major vector of MVE virus, although other mosquitoes, such as *Aedes normanensis* may also be involved.^{1,9}

The last national epidemic of MVE encephalitis occurred in 1974,² beginning in the Murray Valley region of south-eastern Australia. That epidemic included 5 Northern Territory cases, two of which were in the Alice Springs area.¹ A recent review⁸ report that a further 13 cases of MVE disease had been recorded in the Northern Territory between 1975 and 1999, none of which occurred in Central Australia. A single presumptive case from Alice Springs was reported in 1997, but could not be confirmed because of the death of the patient.¹¹ No further cases have been recorded in south-eastern Australia since 1974.

The epidemiology of KUN is less well documented but appears to be more widespread than MVE. It is found throughout northern Australia, with occasional spread to south-eastern Australia,⁷ but cases have never been identified in Central Australia.

Sentinel chicken flocks are employed as a means of early warning of MVE and KUN virus activity by testing for general and specific flavivirus seroconversion.^{12,13} In the months of March and April 2000, a series of media alerts were issued by the Territory Health Services following seroconversion of sentinel chickens in the Northern Territory.

During the same period, clinicians at Alice Springs Hospital reported several cases of undiagnosed neurological illness in both paediatric and adult patients. Eventually 5 cases of MVE and KUN encephalitis were diagnosed in Central Australia.

We report the epidemiology of human disease in Central Australia in 2000, discuss the environmental indicators and public health surveillance systems, and highlight the potential for an ongoing risk to human health.

Patients and methods

Ethical approval was sought from and supported by the Central Australian Human Research Ethics Committee for the publication of the results of this investigation.

The medical records of all 5 cases were reviewed and data on geographical location, age, gender, ethnicity, clinical features, laboratory and radiological investigations were collected.

Serological testing was performed at the Division of Microbiology and Infectious Diseases, Western Australian Centre for Pathology and Medical Research in Perth and in the Arbovirus Research and Surveillance Laboratory, Department of Microbiology, University of Western Australia. A standard flavivirus haemagglutination inhibition (HI) test and an indirect immunofluorescence assay (IFA) were used for IgG and IgM detection in serum and cerebrospinal fluid (CSF) samples.^{3,4} Specific IgG to MVE or KUN was determined using an epitope-blocking enzyme immunoassay (EIA).¹² MVE-RNA in CSF was detected using reverse transcription, then DNA amplification by polymerase chain reaction (RT-PCR).¹⁴ All were done in duplicate and only reported as positive or negative if both results were the same. If the results were discrepant the test was repeated. Samples unable to be resolved on repeat testing were called equivocal.

Data on sentinel chicken seroconversion to MVE and Kunjin viruses in Central Australia were obtained from the Sentinel Chicken Surveillance Programme of the Northern Territory and mosquito vector prevalence data from the Medical Entomology Branch, Northern Territory Department of Health and Community Services. Sentinel flocks are maintained at major population centres by officers of the Northern Territory Department of Primary Industry and Fisheries or by volunteers in a co-operative programme with the Northern Territory Department of Health and Community Services.

They are bled monthly and samples are sent to the Department of Microbiology at the University of Western Australia and tested with the epitope-blocking EIA.¹² Seroconversion of one or more of the flock to MVE virus initiates a media alert by the Northern Territory Department of Health and Community Services.

Mosquito monitoring in the Alice Springs area is carried out on a weekly basis by the Medical Entomology Branch of the Department of Health and Community Services and the Alice Springs Council using 6 sites in urban, semi rural, and rural locations. Mosquito numbers and species are recorded. Increases of potential vector species trigger public health warnings.

Results

The first indication of MVE virus activity in the Northern Territory in 2000 was seroconversion in a sentinel flock in a rural setting near Darwin bled on 24 February. This was followed by sentinel flock seroconversions in Tennant Creek on 3 March and in Alice Springs on 22 March 2000.

From January 2000, there was a sharp rise in *Cx. annulirostris* mosquito numbers at multiple rural sites near Alice Springs in Central Australia. The numbers remained high to very high in most sites until early April, after which numbers began to decline. At the single Alice Springs urban trap site numbers were low to moderate at all times.

All the cases were Aboriginal and came from remote communities. Demographic details are provided in Table 1. Two paediatric patients from a single remote community presented to hospital on the same day, one with MVE encephalitis, and the other with KUN encephalitis. All patients presented with 24-48 hours of prodromal symptoms, including malaise, irritability, fever, vomiting, headache and neck stiffness. In 4 cases there was progression to significant neurological manifestations. Three of these developed severe disease and required ventilation for refractory seizures or deteriorating level of consciousness. One infant was left with residual quadriplegia and one adult with persisting altered consciousness and generalised weakness. A second infant had persistent hypotonia and mild left-sided weakness at 3 month follow-up and has an uncertain neurological outlook. Of the 2 patients considered to have recovered fully, the paediatric patient is neurologically intact, while the adult patient is abnormal but as a result of chronic substance abuse.

Cases 1, 2 and 3 were confirmed as acute MVE encephalitis and case 4 as acute KUN encephalitis (Table 2). Case 5 had a rapid rise in antibody to both viruses with the presence of both KUN and MVE antibody on the epitope-blocking EIA. The CSF showed predominantly polymorphs in children and monocytes in adults. The samples analysed biochemically showed elevated protein and normal glucose.

No cases of non-encephalitic MVE or KUN infection were identified in Central Australia during this period.

Table 1. Demographic and clinical characteristics of the cases

| Case no. | Date of onset | Age | Sex | Symptoms/signs | Outcome | Agent |
|----------|---------------|----------|-----|--|-----------------------------|-----------------------|
| 1 | 25/3/2000 | 69 years | M | Fever, headache, neck stiffness, deteriorating sensorium | Severe cognitive impairment | MVE |
| 2 | 27/3/2000 | 3 months | F | Fever, seizures, flaccid quadriplegia | Quadriplegia | MVE |
| 3 | 3/4/2000 | 2 months | M | Fever, irritability, seizures | Hypotonia | MVE |
| 4 | 3/4/2000 | 4 years | M | Fever, vomiting, neck stiffness | Complete recovery | KUN |
| 5 | 13/4/2000 | 30 years | M | Fever, ataxia, altered sensorium, neck stiffness | Complete recovery | Unspecified (MVE/KUN) |

Table 2. Serology and CSF results, 2000

| Case | Serology | | | | | | | CSF | | | | | |
|------|--------------|------------------|----------------------|------------------|----------------------|--------------|------|-------------|-------------|-------------|----------------|----------|--|
| | Date | MVE HI | MVE IgM | KUN HI | KUN IgM | EIA | Date | PMNs x106/L | Mono x106/L | Protein g/L | Glucose mmol/L | MVE PCR | |
| 1 | 30/3 24/4 | 1:10 1:320 | Positive Positive | <1:10 1:80 | Negative Positive | MVE | 29/3 | 70 | 110 | 0.81 | 3.6 | Equiv* | |
| 2 | 6/4 11/4 | 1:40 1:160 | Positive Positive | 1:80 1:40 | Negative Negative | MVE | 29/3 | 250 | 300 | 2.5 | 3.2 | Positive | |
| 3 | 8/4 28/4 | 1:40 >1:640 | Positive Positive | <1:10 1:320 | Negative Not done | MVE | 5/4 | 510 | 40 | Not tested | Not tested | Not done | |
| 4 | 7/4 3/5 | <1:10 <1:10 | Positive Negative | 1:10 1:160 | Positive Positive | KUN | 8/4 | 110 | 75 | Not tested | Not tested | Not done | |
| 5 | 17/4 4/5 | 1:320 1:10240 | Positive Positive | 1:320 1:20480 | Positive Positive | MVE + KUN | 17/4 | 50 | 140 | 0.94 | 2.3 | Negative | |

Discussion

There had been no confirmed cases of MVE or KUN disease in Central Australia between the last national epidemic in 1974 and this outbreak.⁸ That is presumed to reflect the absence of the correct environmental conditions that would allow the reappearance of the virus, by migration of infected waterbirds into the area or other mechanisms, and the establishment of local cycles of activity.^{1,7,9,10}

The first indicator of MVE activity in Australia in 2000 was seroconversion of sentinel chicken flocks from the Kimberley and Pilbara regions of northern Western Australia, in early January.¹³ This was followed in the Northern Territory by seroconversions in chicken flocks in Darwin in late February, Tennant Creek in early March and Alice Springs in late March, accompanied by a rise in *Cx. annulirostris* mosquito numbers around Alice Springs in January and continued high numbers until early April. These events followed extraordinary environmental conditions, with unusually high rainfall in the preceding months and extensive flooding resulting in large contiguous bodies of water extending from northern Western Australia across to Central Australia (C Woodsworth, Bureau of Meteorology, personal communication; Monthly Weather Review, Bureau of Meteorology). The sequential seroconversion of the sentinel chickens in a south-easterly direction reflected the pattern of rain and flooding, and presumably the migration of MVE and KUN infected birds or wind blown infected vectors aided by prevailing north-westerly monsoonal winds.

The demographic and clinical features in this outbreak were similar to previous reports.^{3,4,5} There was a mixture of adult and paediatric cases that is typical of epidemic disease occurring in non-immune populations,^{3,5} and is consistent with rare flavivirus cases in Central Australia. Interestingly, the cases included 2 young Aboriginal infants. Previous series that included Aboriginal infants^{3,4} had occurred in endemic populations, and there were no cases in children under 6 months of age. This may be due to high levels of maternal antibody expected in these populations^{15,16} providing passive protection for the newborn. That would not have been the case in the Central Australian communities, and therefore very young children were susceptible. The male predominance observed in this series has been previously reported.^{3,4} In adults, it is presumed to reflect higher exposure risk, but it is also seen in young children. The explanation for the latter is unknown.

It is notable that all cases came from remote communities, despite sentinel chicken seroconversion in urban Alice Springs. However, mosquito numbers were low in the urban trap, suggesting that numbers of infected mosquitoes in urban areas were too low to pose a risk to humans despite the presence of the virus in rural areas.

Previous reports from Western Australia (1978-1991) and the Northern Territory (1987-1996) have highlighted the severity of MVE encephalitis.^{3,4,5} Although only 1-2 per 1,000 infections with MVE virus result in encephalitis,¹ of those that do, over 20 per cent are fatal, and permanent neurological sequelae occur in about half the survivors.⁵ With the addition of our 3 definite MVE cases to those summarised previously,⁵ the case fatality rate of MVE is 9/49 (18.4%). Eleven of the 49 (22.4% overall, 27.5% of the survivors) had major neurological sequelae and 12 cases (24.5% overall, 30% of survivors) had minor sequelae. Only 17 cases (34.7%) were documented to have made a complete recovery. All fatalities have occurred in patients less than 2 or over 60 years of age. As previously reported,^{3,4} we found elevated CSF protein in the 3 cases in which it was measured. CSF cell counts showed no clear trends, although the predominance of monocytes in adults and polymorphs in children is of interest, perhaps reflecting earlier sampling in children.

KUN encephalitis is much less common than MVE encephalitis, with only 3 definite cases recorded in the literature since 1974, including the one in this series.^{4,6} In addition, a further confirmed case occurred in Alice Springs in 2001, a 24-year-old woman with a mild illness and full recovery (A Brown and D Smith, personal communication). All of these have survived, suggesting that it may be a milder illness than MVE encephalitis, though the numbers are still too small to be confident.

One of the patients (case 5) had high levels of antibody to both KUN and MVE. It is likely that he had been previously infected with one of these viruses, and the current acute infection evoked brisk antibody responses to both the current and previous virus. We were unable to ascertain which was the current infecting virus. Case 4 showed an initial positive IgM to both MVE and KUN in the serum, but the MVE IgM was quite weak and was not seen in the second sample.

The level of susceptibility to MVE and KUN infection within the Central Australian population is not known, as there is no current local human seroprevalence data. In the absence of cases for

over 25 years, it is assumed that all people who were born or moved into the area since 1974 will be susceptible, including the local Aboriginal community. That is unlike the situation in the Top End where very high levels of past infection are found in local Aboriginal communities.¹⁵ Serosurveys have been conducted in Aboriginal coastal communities in the Cape Leveque region of Western Australia, where occasional human disease occurs.¹⁶ These show low seroprevalence overall with the highest prevalence in the age groups likely to have resided there during the last outbreak in the late seventies and early eighties.³ This suggests that while there may be some effective immunity in people resident in Central Australia during the 1974 epidemic, it is likely to be limited. Therefore it must be assumed that the possibility exists for further outbreaks of MVE in Central Australia in the future, involving both Aboriginal and non-Aboriginal residents and visitors.

A further two cases of MVE encephalitis, one KUN encephalitis and an undifferentiated MVE/KUN encephalitis have occurred the Central Australian region in early 2001 (A Brown and D Smith, personal communication). These occurred around Alice Springs itself and involved Aboriginals and Caucasians. As there was no evidence of spread from outside the area, it suggests that endemic activity has become established in the region. This highlights the need for increased vigilance in the future, particularly in terms of clinical and arboviral surveillance activities, when climatic conditions are ideal for virus replication and transmission. Widespread and high summer rain, high vector mosquito numbers and seroconversion in sentinel chickens in Central Australia may help to predict outbreaks of MVE in Central Australia and other regions, including more densely populated areas of south-eastern Australia. It is believed that epidemics in that area result from reintroduction of virus when 2 successive years of abnormal spring rainfall in the Murray Darling River catchment allow chains of bird-mosquito transmission from northern Australia.⁹ However, if endemic activity is now established in Central Australia, this spread could occur more easily. Prompt and efficient communication between public health authorities, clinicians and the community is essential. Media warnings serve as a reminder for people to take mosquito protection measures, but may also facilitate early diagnosis of clinical cases.

References

1. Marshall ID. Murray Valley and Kunjin encephalitis. In: Monath TP, ed. *The arboviruses: epidemiology and ecology*. Vol III. Boca Raton: CRC Press Inc, 1988:151-189.
2. Bennett NM. Murray Valley encephalitis, 1974: clinical features. *Med J Aust* 1976;2:446-450.
3. Mackenzie JS, Smith DW, Broom AK, et al. Australian encephalitis in Western Australia, 1978-1991. *Med J Aust* 1993;158:591-595.
4. Burrow JNC, Whelan PI, Kilburn CJ, et al. Australian encephalitis in the Northern Territory: clinical and epidemiological features, 1987-1996. *Aust NZ J Med* 1998;28:590-596.
5. Cordova SP, Smith DW, Broom AK, Lindsay MD, Dowse GK, Beers MY. Murray Valley encephalitis in Western Australia in 2000, with evidence of southerly spread. *Comm Dis Intell* 2000;24:368-372.
6. Muller D, McDonald M, Stallman N, King J. Kunjin virus encephalomyelitis. *Med J Aust* 1986;144:41-42.
7. Mackenzie JS, Broom AK, Hall RA, et al. Arboviruses in the Australian region, 1990 to 1998. *Comm Dis Intell* 1998;22:93-100.
8. Spencer JD, Azoulas J, Broom AK et al. Murray Valley encephalitis virus surveillance and control initiatives in Australia. *Comm Dis Intell* 2001;25:33-47.
9. Russell RC. Vectors vs. humans in Australia—who is on top down under? An update on vector-borne disease and research on vectors in Australia. *J Vector Ecol* 1998;23:1-46.
10. Mackenzie JS, Lindsay MD, Coelen RJ, Broom AK et al. Arboviruses causing human disease in the Australasian zoogeographic region. *Arch Virol* 1994;136:447-467.
11. Merritt A, Phillips DA, Carney I, Whelan P. A presumptive case of fatal Murray Valley encephalitis acquired in Alice Springs. *Comm Dis Intell* 1998;22:103-104.
12. Hall RA, Broom AK, Harnett AC, Howard MJ, Mackenzie JS. Immunodominant epitopes on the NS1 protein of MVE and KUN viruses serve as targets for a blocking ELISA to detect virus-specific antibodies in sentinel animal serum. *J Virol Methods* 1995;51:201-210.
13. Sturrock K, Broom A, Van Heuzen B, Lindsay M, Smith D. Seroconversions in sentinel chickens provide an early warning of Murray Valley encephalitis virus activity in Western Australia. *Arbovirus Research in Australia* 2001;8:43-47.
14. Tanaka M. Rapid identification of flavivirus using the polymerase chain reaction. *J Virol Methods* 1993;41:311-322.
15. Holland J, Smith DW, Broom AK, Currie B. A comparison of seroprevalence of arboviral infections between three Northern Territory regions. *Microbiology Australia* 1994;15:A105.
16. Smith DW, Broom AK, Wallace MJ. Prevalence of antibody to Murray Valley encephalitis virus in Aboriginal communities in the Kimberley region of Western Australia in 1995. *Arbovirus Research in Australia* 1997;7:65.
17. Whelan P, Burrow J. Australian encephalitis in the NT. *NT Comm Dis Bull* 1994;2:21-23.

Epidemiology of invasive meningococcal disease in North Queensland, 1995 to 1999

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Abstract

This study describes all episodes of invasive meningococcal disease (n=120) acquired in north Queensland over the 5 year period 1995 to 1999. Indigenous people had a 3-fold greater risk than others of acquiring invasive meningococcal disease. There were 7 deaths, six in non-indigenous people. The majority (72.4%) of identified isolates were serogroup B. We found no evidence of significant resistance to the antibiotics recommended for treatment or chemoprophylaxis. Two outbreaks of disease were identified, one serogroup B and one serogroup C. Compared to the previous 5 years (1990 to 1994) there were far fewer cases of serogroup C disease and a lower incidence and risk of invasive meningococcal disease among indigenous people. *Commun Dis Intell* 2002;26:44-50.

Keywords: invasive meningococcal disease, Neisseria meningitidis, indigenous people

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