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| Watching brief |
| **Title** | 2023 Murray Valley Encephalitis outbreak in Australia |
| **Authors** | Ashley Quigley and Damian Honeyman |
| **Date of first report of the outbreak** | 16 January 20231  |
| **Disease or outbreak** | Murray Valley Encephalitis (MVE) |
| **Origin (*country, city, region*)** | Victoria1, Australia ­ — The first MVE confirmed case of 2023 spent time in Buloke Shire and Swan Hill during her acquisition period1. |
| **Suspected Source (specify food source, zoonotic or human origin or other)** | Murray Valley Encephalitis virus (MVEV) is a mosquito-borne virus. Transmission to humans occurs after a bite from this primary vector that carries the virus. There is no human-human transmission of MVEV. Mosquitoes contract MVEV after feeding on water birds such as herons or egrets2.  |
| **Date of outbreak beginning** | 16 January 20231 - This marks the first human case of MVE in Victoria since the last outbreak in 19743. |
| **Date outbreak declared over** | Ongoing – Seasonal outbreak in 2023. |
| **Affected countries & regions** | Victoria (VIC)1, Northern Territory (NT)4, New South Wales (NSW)5, and Western Australia (WA), Australia. |
| **Number of cases (specify at what date if ongoing)** | As of 6 April, 2023 – 9 cases and 3 deaths have been confirmed in Australia6. **Table 1.** Number of confirmed MVE cases per state as of 6 April, 20236.

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| **State** | **Laboratory Confirmed** | **Probable\*** | **Deaths** |
| VIC | 2 | 1 | 2 |
| NSW | 4 | - | 0 |
| NT | 1 | - | 1 |
| WA | 1 | - | 1 |

\*The second MVE case was later suspected as Japanese encephalitis which has similar clinical presentation but has not yet been confirmed as either - Information not available.Diagnosis of MVEV infection is through molecular testing with MVEV-specific polymerase chain reaction (PCR), serological testing, cerebrospinal fluid testing from lumbar puncture (also known as a spinal tap), and/or testing urine7. Testing can show acute or past infection, however repeat testing is usually required to diagnose MVE on a convalescent sample by assessing rising antibody titres1. |
| **Clinical features** | MVE typically has an incubation period of 1-4 weeks (average, 2 weeks), followed by a prodrome of 2-5 days, often including headaches and high fevers3. Research estimates that between 1 in 150 and 1 in 1000 MVEV infections result in symptomatic disease8,9. If symptomatic, symptoms usually develop 7 to 12 days after being bitten by an infected mosquito, but can be as little as 5 days or as long as 28 days. Symptoms can include10,11: * Fever
* Nausea and vomiting
* Headache
* Muscle aches
* Macular rash
* Cough

People with severe infection may develop the following symptoms1:* Severe headaches
* Neck stiffness
* Sensitivity to bright light (photophobia)
* Seizure or fits (especially in young children)
* Drowsiness
* Confusion
* Seizures
* Loss of consciousness and/or coma

Neurological features occur early and may include lethargy, irritability, and confusion10. Elderly people and children under 5 are most at risk of severe illness. Seizures regularly occur in children and may also occur in adults10,11. A broad spectrum of disease has been reported, including mild cases of encephalitis not requiring hospitalisation, and non-encephalitic cases with fever and headache10. |
| **Mode of transmission (dominant mode and other documented modes)** | MVEV is a mosquito-borne virus that is endemic to Australia, Papua New Guinea and Irian Jaya. MVEV is a member of the Japanese encephalitis serological complex of flaviviruses, which includes Japanese encephalitis virus (JEV), West Nile virus (WNV) and Kunjin virus (KUNV)3. Most MVE cases occur during the wet or post-wet seasons. The primary mosquito vector during epidemics in Australia is *Culex annulirostris,* which are fresh-water breeders native to Australia. *Culex australicus* and some *Aedes* and *Ochlerotatus* mosquito species may also be involved in other aspects of MVE virus ecology1. |
| **Demographics of cases** | People who work, live or spend time outdoors in rural or regional parts of Victoria, NSW and the NT, may be at increased risk of infection. People of all ages are affected by MVE3 and those frequenting inland riverine regions, extending up towards the Murray River may be at increased risk of infection1. In the current outbreak, cases range across all age groups and gender.In Victoria, the first case of MVE was a woman in her sixties who died in late February, whilst the third case is a man in his seventies who is receiving treatment in hospital12. The second MVE case was later confirmed as Japanese encephalitis which has similar clinical presentation, but this has not yet been confirmed. In NSW, the first confirmed MVE case was a man in his 60s, who was admitted to hospital where he continues to receive treatment5. This person was potentially exposed to infected mosquitoes in the Temora Shire, Edward River Shire or Murrumbidgee Council areas, currently NSW areas of MVE concern.The infection was likely acquired in January 2023. The virus has also been detected in a man in his 20s from Federation, NSW, who was likely infected between mid-February and early March 2023. Exposure was thought to have occurred whilst at work in the Federation Shire, or while camping in Indigo Shire in Victoria and currently remains in hospital. The virus has also been detected in a man in his 60s from Leeton Shire, NSW who was infected in March 2023. Exposure was thought to have occurred around home and his local area. He remains admitted to hospital. The fourth NSW cases was confirmed in a man in his 50s in the state's Riverina region who was hospitalised after contracting the virus between January and February. Exposure is unknown at this time13.In Darwin, NT, the only MVE patient was a woman in her 70s who later died from the virus4. In WA, the MVE case recorded was in a child who later died from the virus6. EPIWATCH is an artificial intelligence-driven system harnessing vast, open-source data which generates automated early warnings for epidemics worldwide. Figure 1 shows the statewide distribution of MVE reports from the AI system EPIWATCH, indicating MVE signals at specific time points during the outbreak period. **Figure 1**. The statewide distribution of MVE reports from the AI system EPIWATCH during the outbreak period.  |
| **Case fatality rate** | The reported case fatality rate of MVEV is about 15%–30%14,15. The 2023 MVE Australian outbreak has had a higher mortality rate. In Australia, the CFR for the 2023 outbreak is 37.5%. |
| **Complications** | Severe complications of MVE have been reported with long-term neurological sequelae occurring in 30%–50% of survivors, whilst only 40% of these patients recover completely8,11,14,15. Severe infection may lead to long-term brain damage or death in a proportion of these patients2.  |
| **Available prevention** | Mosquito surveillance and control activities are in place across Australia to reduce the risk of MVE and other mosquito-borne diseases2,5. The best prevention is protection against mosquito bites, by using mosquito prevention methods such as mosquito repellents, cover-up clothing, reducing time spent outdoors in high mosquito periods etc2. |
| **Available treatment** | There is no effective treatment available for MVE, with current treatments aimed to support infected people and ease symptoms. In more severe illness, hospitalisation is needed3.  |
| **Comparison with past outbreaks** | Since first reported in Australia in 1974 from a significant flooding event3, there has been a total of 45 MVE cases with nine reported deaths4. In Victoria, the last recorded human case was reported in 1974. In 2011, cases were recorded in New South Wales and South Australia2.Nationally, MVE risk is highest during the summer months, especially after periods of heavy rainfall or flooding. The wetter than normal conditions lead to increasing numbers of water birds and mosquitoes. This was seen in the 2011 Australian outbreak of MVEV which saw a significant increase in MVEV activity in endemic regions and the re-emergence of MVEV in South-Eastern Australia3. Both these increases in MVEV followed both significant regional flooding and subsequent increased numbers of the predominant mosquito vector, *Culex annulirostris*3. During February 2011, widespread seroconversion among sentinel chicken flocks after heavy rainfall and regional flooding was detected along the Murray River. The 2011 MVEV outbreak resulted in 4 cases and 1 death from the NT, 9 cases and 1 death from WA, 2 cases and 1 death from SA, 1 case from NSW and one suspected but unconfirmed case from VIC. MVEV was subsequently also detected in horses displaying neurological symptoms across South-Eastern Australia during 20113.MVEV has since been detected in VIC and other South-Eastern Australian states in early 2023. Human cases have been confirmed and the virus has been detected in mosquitoes through Arbovirus surveillance. With the upcoming wet 2023 autumn and winter months and as the mosquito and wild bird populations continue to grow and migrate to wetter areas, creating favourable conditions for mosquito-borne disease outbreaks, there is the potential for increased MVE transmission in this 2023 outbreak. The 2022-2023 La Niña season is predicted to end in early 2023 and as Australia prepares to enter El Niño, thereby creating hotter and dryer conditions where stagnant water sources are more susceptible to mosquitoes who require water sources to reproduce, enhanced monitoring for mosquito-borne diseases is essential16. |
| **Unusual features** | The clinical features from presentations of infection with different encephalitic flaviviruses are similar and often overlap. Subsequently, medical professionals struggle to differentiate between these diseases3, particularly JEV and it therefore remains difficult to establish an early diagnosis of MVEV infection. This combined with the lack of proven therapeutic options makes management of MVEV difficult3. In the current Australian outbreak, a higher-than-average CFR for MVE has been observed, with more cases reported in a short span of time than previously observed throughout the 2011 outbreak.Another unusual feature is the demographics of those affected. This is due to different locations, and a change in the demographic pattern of human cases of encephalitic MVEV over the last 20 years. In northern Australia, this is associated with the increasing numbers of non-Aboriginal workers and tourists living and travelling in endemic and epidemic areas, and participating in activities that lead to high mosquito exposure. It is important to note that *Culex tritaeniorhynchus* is the natural vector for JEV and was detected for the first time ever on the mainland in NT in 2019. La Nina was thought to have been a factor in the introduction of *Culex tritaeniorhynchus* to Australia. Three years later, JEV caused an explosive epidemic in animals and humans in 3 states in South-Eastern Australia. In the current outbreak, *Culex annulirostris,* are considered the primary vectors of JEV in Australia, as they yielded >87% of field detections of JEV. *Culex annulirostris* is also considered the primary vector for the current MVE outbreak, and should not be overlooked during sentinel surveillance due to the difficulty in differential diagnosis of both JEV and MVE. |
| **Critical analysis** | In Australia, MVEV was first isolated during a 1951 outbreak, and then subsequently in 1956 and 1974 during major outbreaks17. It is thought that MVEV may be the cause of an unknown outbreaks that occurred in 1922 and 1955. Despite the infrequency of MVEV epidemics, high case numbers have been observed in each outbreak. In 1974, 58 cases of encephalitis were identified18. The outbreaks have consistently occurred predominantly in the South-Eastern parts of Australia. In the 2011 and 2023 outbreaks, cases have been reported in NSW for the first time, with the highest risk of infection occurring between November and March, particularly following significant flooding or periods of lengthy, heavy rainfall1. The last human cases of MVEV infection in VIC were reported in 1974 following a significant flooding event. The same occurred in 2011, where cases were reported after extremely wet conditions.In 2022, Australia experienced heavy rainfall and extensive flooding nationwide. Subsequent increased wild bird populations and growing mosquito numbers provide highly favourable conditions for increased transmission of many mosquito-borne diseases. These include MVE, Japanese encephalitis, Kunjin/West Nile virus, Ross River and Barmah Forest virus infections19. These mosquito-borne viruses are of both many of which are of public and animal health importance. Enhanced surveillance is essential after these significant rainfall events in warmer months, particularly due to the overlap of vector species for both viruses and subsequent increase in mosquito breeding after wetter weather in the warmer months.The *Culex annulirostris* mosquito, which is the primary vector for Flaviviridae transmission in Australia, has also been implicated in JEV transmission globally. Other mosquitoes, such as *Culex australicus* and some *Aedes* and *Ochlerotatus* species, may be involved in other aspects of MVEV ecology1. *Culex tritaeniorhynchus* mosquitoes are not known to transmit MVEV and West Nile virus but have been detected in mosquitoes this 2023 season in multiple jurisdictions in South-eastern Australia where they have not been detected in recent previous years. This could be due to heavy rain and changes in climate, destruction of natural habitats altering bird migratory patterns, agricultural practices, and periurban growth. MVE disease is a ‘notifiable’ communicable disease in all Australian States and Territories, meaning that clinicians and laboratories are required by law to report cases to local health authorities, however, MVE cases could be under-reported as a large proportion of cases asymptomatic, and aetiology is similar to that of JEV. Lessons can be drawn from the JEV serosurvey that was conducted in NSW in 202220. Based on this serosurvey, the proportion of participants with JEV antibodies in their blood samples was 8.7% (80/917) across 5 towns in rural/regional NSW. This is equal to about one infection for every 11 participants. Hence it is possible for a similar situation to be seen for MVE and enhanced sentinel surveillance is recommended.With the potential for a further outbreak of MVEV in the 2023 wet autumn and winter months, the importance of this disease, its clinical characteristics and radiological and laboratory features must be conveyed through public messaging to warn against mosquito-borne diseases and safety measures for their prevention. Real time surveillance and diseases reporting must be performed. |
| **Key questions** | 1. What is the reason for the higher CFR seen in this outbreak, compared to the 1974 and 2011 outbreak?
2. Has increased sentinel surveillance/vector monitoring across all states throughout the year increased detection of MVE cases?
3. How widespread is MVEV in this outbreak compared to past outbreaks?
4. In the current outbreak, has MVEV ben detected in additional mosquito strains in Australia?
5. Will a climatic shift from La Niña to El Niñoproduce more favourable conditions for mosquito-borne diseases? What are the effects of the current weather patterns on MVEV in Australia?
6. Does the JEV vaccine provide any protective effects against MVEV?
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| **References** | 1. Victoria State Government Department of Health. Murray Valley encephalitis. Disease Information and Advice. Published 2023. Accessed March 22, 2023. <https://www.health.vic.gov.au/infectious-diseases/murray-valley-encephalitis>
2. Victoria State Government Department of Health, Better Health Channel. Murray Valley encephalitis. Infections Fact Sheet. Published 2023. Accessed March 22, 2023. <https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/murray-valley-encephalitis>
3. Knox J, Cowan RU, Doyle JS, et al. Murray valley encephalitis: A review of clinical features, diagnosis and treatment. *Medical Journal of Australia*. 2012;196(5):322-326. doi:10.5694/mja11.11026
4. The Guardian. Health alert after woman dies of Murray Valley encephalitis in Northern Territory. Accessed March 22, 2023. <https://www.theguardian.com/australia-news/2023/feb/14/health-alert-as-woman-dies-of-murray-valley-encephalitis-in-northern-territory>
5. NSW Health. First Murray Valley encephalitis case of the season identified in NSW - News. Media Releases. Published 2023. Accessed March 22, 2023. <https://www.health.nsw.gov.au/news/Pages/20230222_00.aspx#:~:text=A%20Murray%20Valley%20encephalitis%20(MVE,in%20the%20state%20since%202011>.
6. Government of Western Australia D of H. WA child from West Kimberley dies of Murray Valley Encephalitis. Media Releases. Published 2023. Accessed April 17, 2023. <https://www.health.wa.gov.au/Media-releases/2023/March/WA-child-from-West-Kimberley-dies-of-Murray-Valley-Encephalitis>
7. Floridis J, McGuinness S, Kurucz N, Burrow J, Baird R, Francis J. Murray Valley Encephalitis Virus: An Ongoing Cause of Encephalitis in Australia’s North. *Trop Med Infect Dis*. 2018;3(2):49. doi:10.3390/tropicalmed3020049
8. ANDERSON SG, DONNELLEY M, STEVENSON WJ, CALDWELL NJ, EAGLE M. Murray-Valley encephalitis; surveys of human and animal sera. *Med J Aust*. 1952;1(4):110-114.
9. Broom AK, Lindsay MDA, Plant AJ, Wright AE, Condon RJ, Mackenzie JS. *EPIZOOTIC ACTIVITY OF MURRAY VALLEY ENCEPHALITIS VIRUS IN AN ABORIGINAL COMMUNITY IN THE SOUTHEAST KIMBERLEY REGION OF WESTERN AUSTRALIA: RESULTS OF CROSS-SECTIONAL AND LONGITUDINAL SEROLOGIC STUDIES*.; 2002.
10. ROBERTSON EG, McLORINAN H. Murray Valley encephalitis; clinical aspects. *Med J Aust*. 1952;1(4):103-107.
11. Burrow JN, Whelan PI, Kilburn CJ, Fisher DA, Currie BJ, Smith DW. Australian encephalitis in the Northern Territory: clinical and epidemiological features, 1987-1996. *Aust N Z J Med*. 1998;28(5):590-596. doi:10.1111/j.1445-5994.1998.tb00653.x
12. Victoria State Government Department of Health. Update on Japanese encephalitis and Murray Valley encephalitis in Victoria. Accessed March 22, 2023. <https://www.health.vic.gov.au/health-alerts/murray-valley-encephalitis-virus-detected-in-victoria>
13. NSW Health. Two more cases of Murray Valley encephalitis detected in NSW. Media Release. Published 2023. [www.health.nsw.gov.au](http://www.health.nsw.gov.au)
14. Mackenzie JS, Smith DW, Broom AK, Bucens MR. Australian encephalitis in Western Australia, 1978-1991. *Med J Aust*. 1993;158(9):591-595. doi:10.5694/j.1326-5377.1993.tb137623.x
15. 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. *Commun Dis Intell*. 2000;24(12):368-372.
16. Seltenrich N. Standing Water and Missing Data: The Murky Relationship between Flooding and Mosquito-Borne Diseases. *Environ Health Perspect*. 2021;129(12):124001. doi:10.1289/EHP10382
17. Miles JAR, Fowler MC, Howes DW. ISOLATION OF A VIRUS FROM ENCEPHALITIS IN SOUTH AUSTRALIA: A PRELIMINARY REPORT. *Medical Journal of Australia*. 1951;1(22):799-800. doi:10.5694/j.1326-5377.1951.tb56527.x
18. Bennett NMcK. MURRAY VALLEY ENCEPHALITIS, 1974: CLINICAL FEATURES. *Medical Journal of Australia*. 1976;2(12):446-450. doi:10.5694/j.1326-5377.1976.tb130324.x
19. Victoria State Government, Agriculture Victoria. First detection of Murray Valley Encephalitis in Victorian mosquitoes. Published 2023. Accessed March 22, 2023. <https://agriculture.vic.gov.au/biosecurity/animal-diseases/vetsource/current-biosecurity-alerts/first-detection-of-murray-valley-encephalitis-in-victorian-mosquitoes#:~:text=17%20January%202023,in%20mosquitoes%20in%20northern%20Victoria>.
20. NSW Health. *Summary of NSW Japanese Encephalitis Virus Serosurvey Results*.; 2022. Accessed June 5, 2023. chrome-extension://efaidnbmnnnibpcajpcglclefindmkaj/https://www.health.nsw.gov.au/environment/pests/vector/Documents/jev-serosurvey-report.pdf

The authors disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Funding was provided by The Balvi Filantropic Fund. |