Emerging Risk Notice

May 2023

Japanese Encephalitis Virus (JEV)

Key Points

- There was a significant change in the distribution of JEV last year in Australia, with a geographic expansion from the northern tip of the country to four southern states.
- JEV is a mosquito-borne flavivirus belonging to Flaviviridae, the same family as West Nile virus, Yellow fever, Murray Valley encephalitis virus, and Saint Louis encephalitis. There is one serotype and five genotypes.[12,13]
- Globally, JEV has been detected in 30 species of mosquitoes belonging to the genera *Aedes, Anopheles, Armigeres, Coquillettidia, Culex*, and *Mansonia.* [13, 14]
- The primary mosquito JEV vectors are *Culex tritaeniorhynchus* (in Asia) and *Culex annulirostris* (in Australia). [14]
- *Culex pipiens*, *Culex quinquefasciatus*, and *Aedes japonicus,* native *U.S. mosquito species,* may be important vectors if JEV were introduced into the United States.[6,14, 18]
- JEV is a zoonotic vector-borne disease that can affect multiple mammalian and bird species including pigs, horses, donkeys, cattle, sheep, goats, dogs, cats, egrets, herons as well as reptiles, amphibians, and humans.[5]
- During the 2021-2022 season, pigs on more than 79 swine farms across four Australian states (South Australia, Victoria, New South Wales, and Queensland) were impacted by JEV; over 40 JEV human infections led to seven deaths. [7, 9, 20, 22, 27]
- JEV was detected for the first time during the 2022-2023 season in New South Wales in November 2022.[11]
- JEV is found throughout Asia, Australia, and Western Pacific Islands; however, Australia observed a geographic spread of JEV last year.[5,12]

Concerns for US Animal Health

- JEV would have a major impact to livestock health, trade, and production as well as public health.[10]
- Potential pathways into the United States are through the introduction of infected mosquitoes and migratory waterbirds and globalized livestock trade.[4,10, 17]
- Competent mosquito vectors and hosts are present in the United States. It has been demonstrated that North American domestic pigs are susceptible to JEV infections.[16, 17]
- JEV primarily affects pigs and horses with between 50 to 70% reproductive losses and low mortality in adult pigs, piglets experiencing up to 100% mortality: and encephalitis in horses with a 0.3% to 30% mortality rate.[5, 9, 10, 12, 14]
- Animals infected with JEV, other than pigs and birds, may exhibit clinical signs, but are considered dead-end hosts where they do not have a high enough viremia for mosquitoes to pick up the virus and transmit to another host.[11]
- JEV control options include treating infected animals, chemical control of vector species, and landscape modifications such as screening barns to reduce vector contact. [5,18]

Epidemiology

Distribution

- JEV is distributed throughout Indonesia, Thailand, Cambodia, Korea, Japan, India, Malaysia, Brunei, Singapore, China, Taiwan, Philippines, Papua New Guinea, Vietnam, Bangladesh, Pakistan, and northern Australia. It has never been detected in the United States.[3, 12]

Hosts

Wildlife Hosts

- Ardeid birds (e.g., herons, egrets; natural reservoirs), can maintain high JEV viremia levels that infect mosquitoes in both rural and urban areas. [1,2, 8,5]

- There are at least 90 different bird species that may be involved in the transmission of JEV. They have a lifelong immunity to the virus after the initial viral infection.[6]

- JEV has been detected in feral swine in Australia in Victoria Daly, Litchfield, Tiwi islands, West Arnhem, Marrakai-Dougalis Daly areas. They can maintain high JEV viremia levels that can infect mosquitoes [9,10, 21]

Domestic Hosts

Swine

- Domestic pigs (amplifying hosts) can maintain high JEV viremia levels that infect mosquitoes in both agricultural and metropolitan areas. [1,2, 8,5]

- Swine symptoms include fetal abnormalities and abortions including mummified and stillborn fetuses, weakness with neurological signs, boar infertility, fluid retention, and congested testicles. [10,14, 18]

- Reproductive loss in domestic swine can be from 50 to 70% with negligible mortality in adult swine.[5]

- High viral titers in swine can last 2 to 4 days. Clinical symptoms can develop in as few as 3 days. Direct transmission via nasal shedding of live virus secretions between pigs has been demonstrated. Infected pigs that survive have a long-lasting immunity to the virus.[6, 14, 15]

- Viral transmission from pig to pig via genetic materials (e.g., semen) is rare.[10]

- JEV can be detected in boar semen.[18]

Equines

- Horses are dead end hosts not capable of transmitting virus to mosquitoes or other animals.[10]

- Incubation period is 4 to 14 days in horses.

- Horse symptoms include fever, jaundice, lethargy, anorexia, and neurological signs may include incoordination, impaired vision, difficulty swallowing.[10]

- Horses may recover in 2 to 3 days. In a severe JEV infection, horses may display high fevers, sweating, wandering, aggressive behavior, blindness, and muscle tremors. Severe JEV infections can result in coma and death. These symptoms are indistinguishable from West Nile virus (WNV) and other encephalitic diseases. [11, 18]

- JEV isolations from horses have been reported in Japan, Hong Kong, Taiwan, and India.[12]

- There have been no confirmed cases of JEV in horses in Australia as of the publication of this notice, but there have been cases where the combination of clinical signs and test results suggest that JEV was possibly the cause of disease.[11]

- A 2003 to 2004 serological study completed in Nepal found JEV sero-prevalence in domestic pigs (48.11%), in ducks (26.79%), and in horses (50%).[15]

Cattle

- Rare JEV clinical cases have been reported in cattle showing neurological signs, fever, depression, decreased appetite and, in some cases, death.[5]

Vectors

- Highly competent mosquito species for JEV transmission are *Aedes albopictus, Aedes vexans, Aedes vigilax, Anopheles tessellatus, Armigeres subalbatus Culex annulus, Culex annulirostris* (main vector in Australia)*, Culex bitaeniorhynchus, Culex fuscocephala, Culex gelidus, Culex pipiens, Culex pipiens pallens, Culex pseudovishnui, Culex quinquefasciatus, Culex sitiens*, *Culex tarsalis, Culex tritaeniorhynchus, and Culex vishnui* [14]

- Mosquito species found in the U.S. that could be JEV competent are *Culex tritaeniorhynchus, Culex tarsalis, Culex annulirostris, Culex gelidus, Culex fuscocephala, Culex vishnui, Culex bitaeniorhynchus, Culex pseudovishnui, Culex whitmorei, Culex sitiens, Culex pipiens molestus, Culex pipiens pipiens, Culex quinquefasciatus, Culex salinarius, Culex nigripalpus, Culiseta inornata, Ochlerotatus dorasalis, Ochlerotatus nigromaculis, Ochlerotatus japonicus, Aedes albopictus, Aedes japonicus, Aedes vexans, Anopheles* spp. and *Mansonia uniformis*.[6, 18]

- Vertical transmission occurs between mosquitoes and their offspring and may be a mechanism that allows for JEV survival through the winter months.[6]

- JEV has been isolated from *Culicoides* species in China.[5]

Pathways

- Geographic expansion of JEV is likely due to human and pig population growth, and changes in land use that may support habitats that are preferred by both bird and mosquito species.[2]

- Introductory pathways to other regions may include bird migration, accidental transportation of mosquito vectors, human movement, and international travel.[2, 9]

- JEV infected mosquito vectors are most likely to enter the United States via aircraft or cargo ships based on a qualitative risk assessment completed in 2018; followed by the authors' 2019 quantitative assessment, which determined the higher risk for infected mosquitoes to enter the United States is via aircraft. [13,19]

Diagnostic Testing

- RT-PCR particularly on central nervous system tissue or fetal tissues. JEV is rarely isolated or detected by PCR in cerebrospinal fluid (CSF). Brain tissue in horses can be used for RT-PCR.[23, 24,25]

- Swine samples can include fetal tissues, fresh brain, tonsil, spleen, blood, or serum. Equine can include fresh brain, CSF, blood, or serum. Isolation/detection of JEV in horses is usually very low so serology can be used to detect antibodies. Currently, the diagnosis of JEV in pigs can be based on virus isolation of central nervous system tissues; viral RNA detection in samples such as blood, brain, and CSF; and/or via the detection of JEV specific antibodies in CSF or serum. In horses, the specimens collected for virus isolation or detection (nucleic acid or antigen) are portions of the corpus striatum, cortex, or thalamus of the brain.

Blood and spinal cord samples can also be used. Due to the short viremia associated with JEV infection (4-5 days) there is a short window for virus detection by PCR in blood and serum samples. [5, 26]

- Pigs seroconvert prior to onset of reproduction signs. High antibody titers in these animals in a single serum sample can be indicative of JEV infection. Detection of specific IgM and IgG in equine cerebrospinal fluid or serum may be suggestive of a current JEV infection.[5]

- The collection of oral/nasal secretion samples from domestic pigs using cotton ropes may be a method to detect JEV positive pigs and appropriate for JEV surveillance in a region. JEV detection in oronasal secretions has potential veterinary diagnostic applications.[17]

- Samples are to be submitted to the National Veterinary Services Laboratories (NVSL). The NVSL Diagnostic Virology Laboratory (DVL) in Ames, IA maintains diagnostics for other flaviviruses, including West Nile Virus. The NVSL Foreign Animal Disease Diagnostic Laboratory (FADDL) at Plum Island, NY is evaluating front-line molecular and confirmatory diagnostic methods.

Treatment

- There are no specific treatments for infected animals beyond treatment for symptoms.[5, 18]

- Live and inactivated vaccines are available for swine and inactivated vaccine for horses; however, no licensed vaccine is available in the United States. [2,5]

Prevention

- Vaccination of equine and swine in endemic areas may be effective. [17, 18]

- Pyrethroids, organophosphates, and carbamates can be used for chemical control of adult mosquitoes.[5,18]

- Landscape modifications may also reduce exposure to mosquito bites such as stabling animals in screened barns, insecticide treated mosquito nets, elimination of waterin outside water-holding containers, and installation of fans in barns. [5,18]

Sources

1. Oliveira ARS, Strathe E, Etchverry I, Cohnstaedt LW, McVey DS, Piaggio J, and Cernicchiaro N. 2018. Assessment of data on vector and host competence of Japanese encephalitis virus: A systematic review of the literature. Preventive Veterinary Medicine 154: 71-89.
2. Erlanger TE, Weiss S, Keiser J, Utzinger J, Wiedenmayer K. 2009. Past, present, and future of Japanese encephalitis. Emerging Infectious Diseases 15(1) 1-7.
3. Filgueira L and Lannes N. 2019. Review of Emerging Japanese virus: New Aspects and Concepts about Entry into the Barn and Inter-Cellular Spreading. Pathogens 8 (111): 1-19.
4. Oliveria ARS, Cohnstaedt LW, Noronha LE, Mitzel D, McVey DS, and Cernicchiaro N. 2020. Perspectives Regarding the Risk of Introduction of the Japanese Encephalitis Virus in the United States. Frontiers in Veterinary Science 7:48
   Spickler, Anna Rovid. 2016. *Japanese Encephalitis*. Retrieved from http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php
5. Oliveira ARS, Cohnstaedt LW, and Cernicchiaro N. 2018. Japanese Encephalitis Virus: Placing Disease Vectors in the Epidemiologic Triad. Annals of the Entomological Society of America. 111: 295-303.
6. Hurk van den AF, Pyke AT, Mackenzie JS, Hall-Medelin S, and Ritchie SA. 2019. Japanese Encephalitis Virus in Australia: From Known Known to Known Unknown. Tropical Medicine and Infectious Disease 4(38): 1-11.
7. Lindahl JF, Stahl K, Chirico J, Boqvist S, Thu HTV, and Magnusson U. 2013. Circulation of Japanese Encephalitis virus in Pigs and Mosquito vectors within Can Tho City, Vietnam. Negal Tropical Diseases 7(4): e2153
8. Japanese Encephalitis Virus Detected in Australia's Feral Pig Herd. Ag Web Farm Journal, Jennifer Shike, April 8,2022.https://www.agweb.com/news/livestock/pork/japanese-encephalitis-virus-detected-australias-feral-pig-herd
9. Japanese encephalitis in animals. Northern Territory Government Australia. Updated 16 June 2022. https://nt.gov.au/industry/agriculture/livestock/animal-health-and-diseases/japanese-encephalitis-in-animals.
10. Japanese encephalitis virus. https://www.agriculture.gov.au/biosecurity-trade/pests-diseases-weeds/animal/japanese-encephalitis. Accessed page 14 March 2023
11. Gulati BR, Singha H, Singh BK, Virmani N, Kumar S, and Singh RK. 2012. Isolation and genetic characterization of Japanese encephalitis virus from equines in India. J. Vet Sci. 13(2): 11-118.
12. Oliveira A RS., Piaggio J., Cohnstaedt LW, McVey S., and Cernicchiaro N. 2018. A quantitative risk assessment (QRA) of the risk of introduction of the Japanese encephalitis virus (JEV) in the United States via infected mosquitoes transported in aircraft and cargo ships. Preventive Veterinary Medicine 160: 1-9.
13. Van den Eynde C., Sohier C., Matthijs S., and De Regge N. 2022. Japanese Encephalitis Virus Interaction with. Mosquitoes: A Review of Vector Competence, Vector Capacity, and Mosquito Immunity. Pathogens 11:317
14. Pant G. 2006. A serological survey of pigs, horses, and ducks in Nepal for evidence of infection with Japanese Encephalitis virus. Ann. N.Y. Acad. Sci. 1081:124-129.
15. Park SL, Huang YJS, Lyons AC, Ayers VB, Hettenbach SM, McVey DS, Burton KR, Higgs S, Vanlandingham DL. 2018. North American domestic pigs are susceptible to experimental infection with Japanese encephalitis virus. Scientific Reports 8:7951.
16. Park SL, Huang YJS, and Vanlandingham DL. 2022. Re-examining the importance of pigs in the transmission of Japanese encephalitis virus. Pathogens 11:575.
17. Japanese Encephalitis Virus. Factsheet. Swine Health Information Center. July 2021.
18. Oliveria ARS, Piaggio J, Cohnstaedt LW, McVey DS, and Cernicchiaro N. 2019. Introduction of the Japanese encephalitis virus (JEV) in the United States – A qualitative risk assessment. Transboundary Emerging Diseases 66:1558-1574.
19. Drake J. 2022. What You Need to Know about the outbreak of Japanese Encephalitis in Australia. Science. https://www.forbes.com/sites/johndrake/2022/06/13/what-you-need-to-know-about-the-outbreak-of-japanese-encephalitis-in-australia/?sh=504fc7f01f43.
20. Gentle M, Wilson C, and Cuskelly J. 2022. Feral Pig management in Australia: implications for disease control. Australian Veterinary Journal 1-4. doi: 10.1111/avj.13198
21. Waller C, Currie BJ, Williams DT, Baird RW. 2022. Japanese encephalitis in Australia – A Sentinel Case. N Engl J Med; 387:661-662 DOI: 10.1056/NEJMc2207004
22. Lam M K.H.K., Ellis T.M., Williams D.T., Lunt R.A., Daniels P.W., Watkins K.L. & Riggs C.M. 2005. Japanese encephalitis in a racing thoroughbred gelding in Hong Kong. Vet. Rec. 157: 168.
23. Lian W.C., Liau M.Y. and Mao C.L. 2002. Diagnosis and genetic analysis of Japanese encephalitis virus infected in horses. J. Vet. Med. B Infect. Dis. Vet. Public Health 49: 361–365.
24. Mansfield KL, Hernandez-Triana LM, Banyard AC, Fooks AR, Johnson N. 2017. Japanese encephalitis virus infection, diagnosis, and control in domestic animals. Vet Microbiol. 201:85-92. doi:10.1016/j.vetmic.2017.01.014
25. Chapter 3.1.10. Japanese encephalitis. In Manual of Diagnostic Tests and Vaccines for Terrestrial Animals 2021; World Organization for Animal Health (OIE)
26. Mackenzie JS and Williams DT. 2022. Japanese encephalitis virus: an emerging and re-emerging virus in Australia. Microbiology Australia 43(4): 150–155