DISEASE RESPONSE STRATEGY JAPANESE ENCEPHALITIS

FAD PReP
Foreign Animal Disease Preparedness & Response Plan

United States Department of Agriculture

United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

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Preface

The *Disease Response Strategy: Japanese Encephalitis* provides strategic guidance for responding to an animal health emergency caused by Japanese encephalitis virus (JEV) in the United States.

This *Disease Response Strategy: Japanese Encephalitis* was last updated in **July 2024**. Please send questions or comments to:

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Introduction

Japanese Encephalitis (JE) is a World Organisation for Animal Health (WOAH) notifiable disease due to its potential for international spread, impact on livestock health and production, and ability to cause severe illness in humans. JE is a significant public health risk, causing approximately 68,000 cases and 13,600–20,400 deaths in humans (primarily children) annually[1]. This *Disease Response Strategy: Japanese Encephalitis* was drafted in recognition of the disease's importance to both animal and human health. This document is intended to provide a broad overview of strategy for USDA, APHIS, and responders at all levels in the event of a JE outbreak, should it enter the United States. This overview covers the pertinent etiology and ecology of JE as well as general response strategies. Further information and in-depth reviews of JE can be found in the references and resources section at the end of this document.

This document does not cover, in detail, incident coordination or general foreign animal disease (FAD) response. For more information on these aspects of the response, please refer to the *APHIS Foreign Animal Disease Framework: Roles and Coordination (FAD PReP Manual 1-0)* and the *APHIS Foreign Animal Disease Framework: Response Strategies (FAD PReP Manual 2-0)*. These documents cover general roles and responsibilities as well as general FAD response strategies, respectively.

Additionally, this document does not provide, in detail, every response policy or response procedure for a JE outbreak. There will be additional policy guidance provided during a JE outbreak on specific response operation activities, tailored to the conditions of the outbreak. Finally, this document does not address ongoing management should JE become established in the United States.

Nature of the Disease

JE is an arthropod-borne viral disease of swine, equids, birds, and humans. The disease is caused by the Japanese encephalitis virus (JEV), a positive-strand, Ribonucleic Acid (RNA) virus that belongs to the *Flavivirus* genus in the Flaviviridae family. It is a member of a serological group that includes West Nile virus (WNV), Saint Louis encephalitis virus (SLEV), and five other viruses that together occur on every continent except Antarctica.[2] Globally, this zoonotic disease is known to cause around 70,000 cases of human encephalitis each year. JE also causes significant reproductive losses in swine and encephalitis in horses.

There is only one known serotype of JEV, but at least five genotypes have been identified through sequencing of the viral pre-membrane region. Many different species are susceptible to natural JEV infection: swine (feral and domestic), equids (primarily horses), birds (wild and domestic species), cattle, sheep, goats, dogs, cats, wild mammals, reptiles, amphibians, and humans. All animals except swine and birds are considered dead-end hosts; in other words,

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[1] World Health Organization (2019, May). *Japanese Encephalitis*. https://www.who.int/news-room/fact-sheets/detail/japanese-encephalitis.

[2] Khare B. & Kuhn R.J. (2022). The Japanese Encephalitis Antigenic Complex Viruses: From Structure to Immunity. *Viruses*, 14(10), 2213. https://doi.org/10.3390/v14102213.

animals experience infections with viremia levels too low to contribute to transmission to other animals or humans.[3]

JEV is endemic throughout south and southeastern Asia and portions of the Western Pacific. Its reach extends to the Indian subcontinent, as far west as Pakistan and as far south as northern Australia. In 2021-2022, JEV emerged in southeastern Australia where widespread transmission occurred, and the source of introduction has yet to be determined as of the writing of this Strategy.[4] JEV has never been found in the United States.

Transmission and Reservoirs

JEV is transmitted through the bite of a mosquito, typically of the *Culex* genus. In Asia, *Culex tritaeniorhynchus*, *Cx. vishnui*, *Cx. pseudovishnui*, *Cx. gelidus*, and *Cx. fuscocephala* have been specifically implicated. In the Western Pacific, including Australia, *Culex annulirostris* is considered the primary vector of JEV.[3] In the United States, *Cx. tarsalis* and *Cx. pipiens* are the primary vectors for transmission of endemic flaviviruses. *Cx. pipiens*, *Cx. quinquefaciatus, Cx. tarsalis, Aedes albopictus, Aedes vexans,* and *Aedes japonicus*, which have been shown to be competent vectors of JEV, are the most likely species to serve as vectors if JEV were introduced into the United States.[5,6]

The virus is maintained in a transmission cycle between the mosquito vector and vertebrate hosts, predominantly swine or ardeid wading birds (such as herons and egrets). While ardeid birds have been implicated in multiple studies as the natural reservoir, birds from a variety of different species have been shown to be susceptible to infection with JEV but are considered to play a minor role in virus transmission. Young chicks and ducklings have been experimentally shown to develop sufficient viremia to infect mosquitoes.[7] However, their role in natural transmission cycles remains unclear.

Swine and ardeid birds serve as amplifying and maintenance hosts due to their high viremia. The mechanism of maintenance through the winter in temperate regions is unknown but is suspected to be related to infected hibernating mosquitoes, transovarial passage, or maintenance in

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[3] Van den Eynde, C., Sohier, C., Matthijs, S., & De Regge, N. (2022). Japanese Encephalitis Virus Interaction with Mosquitoes: A Review of Vector Competence, Vector Capacity and Mosquito Immunity. *Pathogens*, 11, 317. https://doi.org/10.3390/pathogens11030317.
[4] Williams, C.R., Webb C.E., Higgs, S., & van den Hurk, A.F. (2022). Japanese Encephalitis Virus Emergence in Australia: Public Health Importance and Implications for Future Surveillance. *Vector Borne Zoonotic Disease*, 22(11), 529-534. https://doi:10.1089/vbz.2022.0037.
[5] Van den Eynde, C., Sohier, C., Matthijs, S., & De Regge, N. (2022). Japanese Encephalitis Virus Interaction with Mosquitoes: A Review of Vector Competence, Vector Capacity and Mosquito Immunity. *Pathogens*, 11, 317. https://doi.org/10.3390/pathogens11030317.
[6] Riad, M.H., Scoglio, C., McVey, D.S., et al. (2017). An individual-level network model for a hypothetical outbreak of Japanese encephalitis in the USA. *Stochastic Environmental Research and Risk Assessment*, 31, 353–367. https://doi.org/10.1007/s00477-016-1353-0.
[7] Cleton, N. B., Bosco-Lauth, A., Page, M. J., & Bowen, R. A. (2014). Age-related susceptibility to Japanese encephalitis virus in domestic ducklings and chicks. *The American Journal of Tropical Medicine and Hygiene*, 90(2), 242–246. https://doi.org/10.4269/ajtmh.13-0161.

amphibians, reptiles, or bats.[8]

In an experimental setting, vector-free transmission has been documented in pigs via oronasal shedding in an experimental setting, but this has not been substantiated in field studies. The significance of direct transmission in natural infection remains unclear.[9] Artificial insemination practices may lead to transmission as infection may cause inflammation of the genital tract in boars and subsequent shedding of the virus in semen[10].

Horses and humans do not play an important role in the natural spread of JEV and are regarded as dead-end hosts, since the viremias they develop are insufficient to pass on the infection to mosquitoes (i.e., horses and humans do not maintain high enough viral titers to infect biting mosquitoes).[11] There has been no evidence that contact, such as two horses sharing a feed bucket, will result in JEV transmission.

Humans primarily become infected through the bite of a mosquito. In a laboratory setting, JE virus might be transmitted through accidental percutaneous exposure, or theoretically, mucosal or inhalational exposure.[12]

Incubation Period[13, 14]

The incubation period for JE in horses is between 8–10 days. For experimentally infected swine, signs of infection, fever, and viremia were observed 24 hours post inoculation with other clinical manifestations apparent within 3 days post inoculation. For the purposes of the World Organisation for Animal Health (WOAH) Terrestrial Code, the incubation period for JE is 21 days.

Clinical Signs, Morbidity, and Mortality

Horses[14]

Infection is most often inapparent with clinical cases occurring infrequently and varying in severity. Subclinical cases are the most common. The WOAH Technical Disease Card for JE describes three syndromic manifestations: transitory, lethargic, and hyperexcitable.

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[8] World Organisation for Animal Health. (2019). *Japanese Encephalitis Technical Disease Card*. https://www.woah.org/app/uploads/2021/03/japanese-encephalitis.pdf.

[9] Park, S.L., Huang, Y.-J.S., & Vanlandingham, D.L. (2022). Re-Examining the Importance of Pigs in the Transmission of Japanese Encephalitis Virus. *Pathogens*, 11, 575. https://doi.org/10.3390/pathogens11050575.

[10] Ogasa A, Yokoki Y, Fujisaki Y, Habu A. (1977). Reproductive disorders in boars infected experimentally with Japanese encephalitis virus. *Jap J Anim Reprod,* 23, 171–175.

[11] Mulvey, P., Duong, V., Boyer, S., *et al*. (2021). The Ecology and Evolution of Japanese Encephalitis Virus. *Pathogens*, 10, 1534. https://doi.org/10.3390/pathogens10121534.

[12] Hills S.L., Walter E.B., Atmar R.L., Fischer M. (2019). Japanese Encephalitis Vaccine: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep,* 68(No. RR-2), 1–33. http://dx.doi.org/10.15585/mmwr.rr6802a1.

[13] World Organisation for Animal Health. (2000). *Terrestrial Animal Health Code Article 8.10*. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/?id=169&L=1&htmfile=chapitre_japanese_encephalitis.htm.

[14] World Organisation for Animal Health. (2019). *Japanese Encephalitis Technical Disease Card*. https://www.woah.org/app/uploads/2021/03/japanese-encephalitis.pdf.

Horses affected by the transitory type may experience fever, anorexia, lethargy, impaired locomotion, and congested or jaundiced mucosal membranes; most recover in 2–3 days.

Those affected by the lethargic-type syndrome may display neurologic signs (in addition to signs attributed to the transitory type) such as difficulty swallowing, lack of coordination (ataxia), and impaired vision, most recover in about a week.

The most severe form, the hyperexcitable type, is characterized by high fever, profuse sweating, and neurological signs such as aimless wandering, aggressive or wild behavior, blindness, and muscle tremors. The hyperexcitable type may result in collapse, coma, and death. Should the horse recover, neurological problems may persist.

In horses, morbidity rates have been reported from less than 1 percent to just over 1 percent; case fatality rates are typically 5 percent to 15 percent but can reach 30-40 percent.

Swine[13]

Although JEV typically causes subclinical infection in swine, reproductive disease is the most characteristic clinical manifestation. Reproductive failures and piglet mortality may result in production losses. Stillborn or mummified fetuses delivered at full term are most common. Abortions and piglets born with muscle tremors/convulsions followed by piglet death are also signs of JE. Among swine, reproductive losses can reach 50–70 percent and mortality in non-immune infected piglets may reach nearly 100 percent. Other signs of JE include infertility in boars that may be permanent depending on the severity of the illness.

Swine that are not pregnant do not typically show signs of infection or experience only mild transient fever. Encephalitis is occasionally observed in naïve swine under 6 months of age. Mortality rates are close to zero for adult swine.

Cattle

The clinical presentation in cattle is similar to horses, in that most infections of JEV are subclinical.[15] If clinical signs are observed they could include anorexia, depression, and/or neurologic signs and potentially abortion.[16,17] There are limited case reports of JEV infection in cattle and more studies are needed.

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[15] Kuwata, R., Sugiyama, H., Yonemitsu, K., Van Dung, N., Terada, Y., Taniguchi, M., … & Maeda, K. (2015). Isolation of Japanese encephalitis virus and a novel insect-specific flavivirus from mosquitoes collected in a cowshed in Japan. *Archives of Virology*, 160, 2151-2159.

[16] Kako, N., Suzuki, S., Sugie, N., Kato, T., Yanase, T., Yamakawa, M., & Shirafuji, H. (2014). Japanese encephalitis in a 114-month-old cow: pathological investigation of the affected cow and genetic characterization of Japanese encephalitis virus isolate. *BMC Veterinary Research*, 10, 1-8.

[17] Mansfield, K. L., Hernández-Triana, L. M., Banyard, A. C., Fooks, A. R., & Johnson, N. (2017). Japanese encephalitis virus infection, diagnosis and control in domestic animals. *Veterinary Microbiology*, 201, 85-92.

Humans[18]

Most infections are asymptomatic. In those who develop clinical signs, illness usually begins with fever and headache which may progress to mentation changes, focal neurologic deficits, weakness, and movement disorders. Severe neurological signs such as flaccid paralysis and Parkinsonian syndrome can occur. Neurologic complications are common in survivors of severe disease.

Less than 1 percent of all infections with JEV result in clinical disease. Case fatality rates typically range from 20 to 30 percent, with neurologic sequelae in up to 50 percent of survivors.

Differential Diagnosis

When considering a potential diagnosis of JE in the United States the list of possible differential diagnoses includes but is not limited to:[19]

Horses

** indicates a foreign animal disease*

- African horse sickness*
- babesiosis (equine piroplasmosis)*
- bacterial encephalitis
- toxic encephalopathies
- Borna disease*
- botulism
- cerebral nematodiasis or protozoodiasis
- equine herpesvirus myeloencephalopathy
- equine infectious anemia
- equine protozoal myeloencephalitis
- hepatic encephalopathy
- leucoencephalomalacia (*Fusarium moniforme*)
- other viral encephalitides, including but not limited to
    - Eastern equine encephalitis
    - Murray valley encephalitis*
    - Western equine encephalitis
    - Venezuelan equine encephalitis*
    - West Nile encephalitis
- rabies
- tetanus
- viral equine rhinopneumonitis

[18] Centers for Disease Control and Prevention. (2022, October). *Japanese Encephalitis Virus: Clinical and Laboratory Evaluation*. U.S. Department of Health and Human Services. https://www.cdc.gov/japaneseencephalitis/healthcareproviders/healthcareproviders-clinlabeval.html.
[19] World Organisation for Animal Health. (2019). *Japanese Encephalitis Technical Disease Card*. https://www.woah.org/app/uploads/2021/03/japanese-encephalitis.pdf.

Swine

** indicates a foreign animal disease*

- blue-eye disease (porcine rubulavirus)
- brucellosis
- classical swine fever*
- coronavirus
- encephalomyocarditis virus
- hemagglutinating encephalomyelitis
- Menangle virus
- other causative agent of SMEDI (stillbirth, mummification, embryonic death, and infertility)
- porcine parvovirus
- porcine reproductive and respiratory syndrome
- pseudorabies
- Teschen/Talfan
- water deprivation/excess salt
- viral/fever induced abortion

Cattle

- Due to the vague clinical signs of disease presentation specific differential diagnosis could vary greatly and could include:
  - Encephalopathies
  - Rabies
  - Tetanus
  - Intoxications
  - Viral induced abortion
  - Water deprivation/excess salt

Laboratory Diagnosis

The World Organisation for Animal Health *Manual of Diagnostic Tests and Vaccines for Terrestrial Animals Chapter 3.1.10* outlines diagnostic laboratory methods for JE. Please refer to the Diagnostics Section in this Response Strategy for details on testing in the United States in the event of an outbreak.

Vaccination and Treatment

There is not currently a USDA-licensed vaccine available for horses, swine, or cattle in the United States. In endemic countries, modified live and inactivated vaccines are available for swine and inactivated vaccines are available for horses. The vaccine for horses is prepared by formalin-inactivation of a virus suspension derived from cell cultures. In swine both inactivated and live-attenuated vaccines derived from cell cultures are used.[20] The vaccines available for

[20] World Organisation for Animal Health. (2019). *Japanese Encephalitis Technical Disease Card*. https://www.woah.org/app/uploads/2021/03/japanese-encephalitis.pdf.

horses and swine are thought to be protective against all genotypes of JEV though efficacy may vary.[21] Vaccination of swine, the amplifying hosts, benefits horses and humans by decreasing the viral titers of swine, thereby reducing the transmission of JE. It also serves to prevent reproductive losses in swine. Vaccination of horses prevents clinical disease and possible sequelae.

While a study in Japan indicated that JEV-vaccinated horses can produce false-positive results in West Nile Virus (WNV) serological testing, it is unknown whether previous WNV vaccination (or infection) is protective against JEV infection in horses.[22]

Several vaccines are available for humans in endemic countries. IXIARO® (Valneva GmbH), an inactivated vaccine derived from Vero cells, is available for humans in the United States. It is approved for individuals 2 months of age and older as a 2-dose series; doses are administered 28 days apart with the last dose administered at least 1 week prior to travel.[23] For adults aged 18–65 years, the two doses can be administered in an accelerated schedule at an interval of 7–28 days.

Treatment in humans and animals is supportive; there is no specific antiviral therapy available.[24] Survivors of natural infection, both animal and human, are thought to acquire long-lasting immunity.

Persistence of JEV[25]

JEV is inactivated by changes in temperature, pH, exposure to various chemicals and disinfectants as well as environmental impacts, as outlined in Table 1.

Table 1. Resistance to Physical and Chemical Action of Japanese Encephalitis Virus.

Action	**Resistance**
Temperature	Destroyed by heating for 30 minutes above 56 °C (132.8 °F); thermal inactivation point is 40 °C (104 °F).
pH	Inactivated in acid environment of pH 1–3 (stable in alkaline environment of pH 7–9).
Chemicals/disinfectants	Inactivated by organic and lipid solvents, common detergents, iodine, phenol iodophors, 70% ethanol, 2% glutaraldehyde, 3–8% formaldehyde, 1% sodium hypochlorite.
Environment	Virus very labile and does not survive well in environment; sensitive to ultraviolet light and gamma irradiation.

[21] Spickler, A.R. (2016). *Japanese Encephalitis*. Center for Food Security and Public Health. http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php.
[22] Hirota, J., Nishi, H., Matsuda, H., et al. (2010). Cross-reactivity of Japanese Encephalitis Virus-Vaccinated Horse Sera in Serodiagnosis of West Nile Virus. *Journal of Veterinary Medical Science*, 72(3), 369-372. https://doi.org/10.1292/jvms.09-0311.
[23] Centers for Disease Control and Prevention. (2023, February). *Japanese Encephalitis Virus: Japanese Encephalitis Vaccine*. U.S. Department of Health and Human Services. https://www.cdc.gov/japanese-encephalitis/hcp/vaccine/index.html.
[24] Spickler, A.R. (2016). *Japanese Encephalitis*. Center for Food Security and Public Health. http://www.cfsph.iastate.edu/DiseaseInfo/factsheets.php.
[25] World Organisation for Animal Health. (2019). *Japanese Encephalitis Technical Disease Card*. https://www.woah.org/app/uploads/2021/03/japanese-encephalitis.pdf.

Criteria for Disease Freedom/Trade Implications

WOAH does not grant official recognition for JE-freedom, but as a member of WOAH, the United States can self-declare the entire country, zone, or compartment free of JE. Criteria for self-declaration of disease freedom are outlined in the WOAH Terrestrial Animal Health Code, Chapter 1.6. Surveillance of susceptible animals, reservoir hosts, and mosquito vectors will likely be required to demonstrate disease freedom. In the case of JE, eradication is unlikely making a disease freedom declaration also unlikely.

WOAH recommends importation restrictions on live horses from countries or zones affected with JE but does not address trade restrictions for swine.[26] Trading partners determine whether to implement, lift, or modify trade restrictions based on negotiations and information that is provided by the United States.

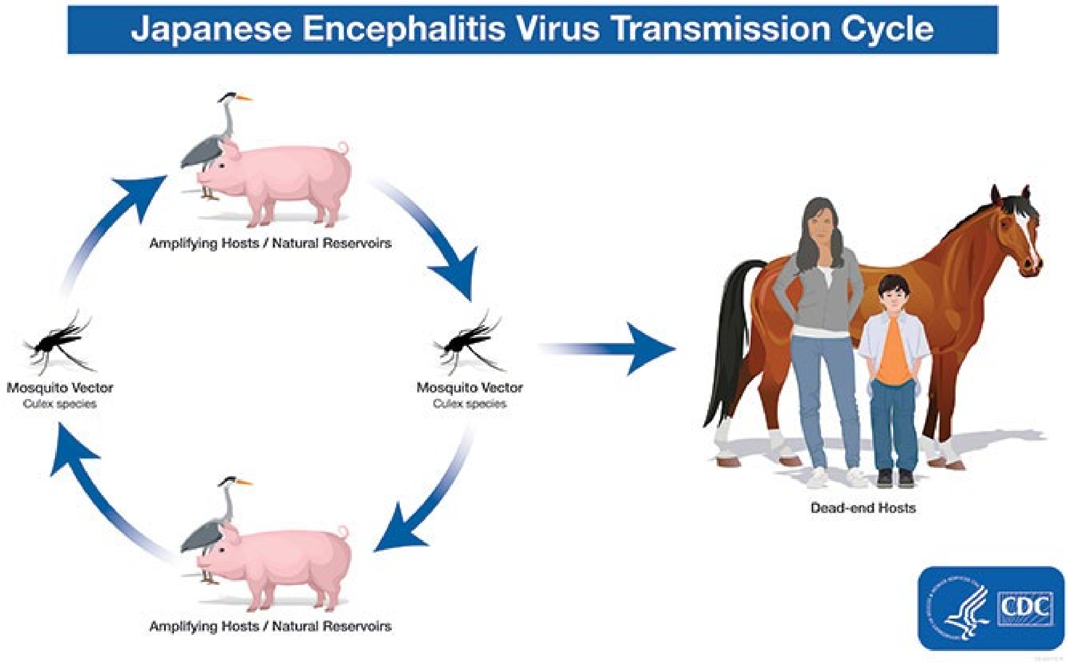
One Health Approach

One Health is a collaborative, multisectoral, and transdisciplinary approach – working at the local, regional, national, and global levels – with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.

Responding to a potential introduction of JEV in the United States will require a One Health approach, as indicated in Figure 1, with collaboration across the animal, human, and environmental health sectors. APHIS will coordinate response activities closely with the Department of Health and Human Services (HHS) Centers for Disease Control and Prevention (CDC), the Department of Homeland Security (DHS), the Environmental Protection Agency (EPA), as well as state, local, tribal, and territorial (SLTT) partners from animal health (domestic and wild), public health, and environmental agencies.

[26] World Organisation for Animal Health. (2000). Terrestrial Animal Health Code Article 8.10. https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/?id=169&L=1&htmfile=chapitre_japanese_encephalitis.htm.

Figure 1. Depiction of the connections between transmission to/from humans, animals, and the environment (wild animals).



APHIS supports timely and open communication and information sharing among sectors and with non-governmental partners from academia, industry, and non-governmental organizations. Elements of this response strategy, including surveillance, vector control, carcass disposal, and wildlife management will only be possible using this One Health approach.

Response Strategy

JEV could enter the United States via several pathways; the highest risk has been assessed to be from the transportation of infected mosquitoes via aircraft. Other routes of entry, including via infected birds or other animal hosts, vaccines, or other biologics, are estimated to pose a negligible risk under current conditions[27]. If JEV was introduced to the United States, detection likely would be delayed due to the low index of suspicion for JE among veterinarians and healthcare providers (due to endemic diseases with similar clinical signs), and the potential cross-reactivity between JEV and other flaviviruses in serologic tests. This detection delay would increase the likelihood that an enzootic transmission cycle would be established prior to detection. Transmission in wild birds along with a large number and wide range of potential hosts and mosquito vectors present in the United States would make achieving eradication of JE difficult.

[27] Oliveira, A. R. S., Cohnstaedt, L. W., Noronha, L. E., Mitzel, D., McVey, D. S., & Cernicchiaro, N. (2020). Perspectives Regarding the Risk of Introduction of the Japanese Encephalitis Virus (JEV) in the United States. Frontiers in veterinary science, 7, 48. https://doi.org/10.3389/fvets.2020.00048.

In the United States, JE is a Foreign Animal Disease (FAD) and a notifiable disease. Suspect cases should be reported to a State Animal Health Official or Area Veterinarian-in-Charge. For more information on conducting FAD investigations please refer to the *APHIS Foreign Animal Disease Framework: Investigation Manual (FAD PReP Manual 4- 0)*.

Response options will be determined based upon the circumstances of JEV introduction in the United States, taking into consideration a variety of factors such as species affected, geographic distribution, and region of introduction. APHIS response efforts will focus on control of JE in domestic animal populations as needed to protect public health and to support the swine and equine industries. APHIS and CDC will coordinate closely in their roles leading the animal and public health responses, respectively.

Case Definitions

The case definition for JE is available on the APHIS National List of Reportable Animal Diseases webpage. The link is provided to ensure that the most up-to-date case definition is referenced in this Strategy.

The current confirmed case definition for JE, as of 2024, requires virus isolation and/or identification through sequencing at the National Veterinary Services Laboratories (NVSL).

Surveillance

Currently there is no active surveillance for JE being conducted in the United States in mosquitoes, swine, equids, or birds. JE surveillance among humans focuses on cases among international travelers and about one JE case per year is reported to the National Notifiable Disease Surveillance System[28].

In the event of a JE detection in livestock in the United States, a surveillance plan will be developed according to the *National Animal Health Management System (NAHEMS) Guidelines: Surveillance, Epidemiology, and Tracing*. Existing passive and active surveillance mechanisms for endemic arboviral diseases could be leveraged for JE surveillance, such as CDC's ArboNET. Passive surveillance for endemic arboviral diseases, including West Nile, St Louis encephalitis, and eastern equine encephalomyelitis, could potentially identify JEV infection in a horse, human, or bird. Active arboviral surveillance in mosquitoes could be expanded to potentially identify JEV infection. Mosquito surveillance in the United States is generally conducted at the county or local level by public health and environmental health officials. APHIS will coordinate closely with CDC, state, and local jurisdictions on surveillance efforts.

[28] Janatpour ZC, Boatwright MA, Yousif SM, Bonilla MF, Fitzpatrick KA, Hills SL, Decker CF. (2023). Japanese encephalitis in a U.S. traveler returning from Vietnam, 2022. Travel Med Infect Dis, 52, 102536. https://doi.org/10.1016/j.tmaid.2022.102536.

Diagnostics

The National Veterinary Services Laboratories, Foreign Animal Disease Diagnostic Laboratory (NVSL-FADDL), has assessed an reverse transcription-quantitative polymerase chain reaction (RT-qPCR) assay capable of detecting JEV genotypes I-IV, including genotype IV from the 2022 Australian outbreak. Diagnostic testing for animals displaying clinical signs suggestive of JEV would be provided at no cost to animal owners and producers at the NVSL in Ames, Iowa during the initial response. National Animal Health Laboratory Network (NAHLN) labs can provide testing for JEV, but confirmatory testing would need to be completed by NVSL. Veterinarians and producers must first notify their State or Federal Animal health officials if JE is on a differential list, and these officials will assist in the submission and sampling as needed.

The usefulness of serology in animals is limited due to known cross-reactivity with endemic viruses. Thus, initially, serology will not be offered as an on-demand diagnostic test at NVSL. NVSL uses both polymerase chain reaction (PCR) and sequencing to identify and confirm the presence of JEV. Acceptable sample types for pigs include fresh brain, tonsils, spleen, ethylenediamine tetraacetic acid (EDTA) blood, or serum, as well as aborted fetal brain. For horses, acceptable sample types include fresh brain, cerebrospinal fluid, EDTA blood, or serum. Collect and submit as many of the suggested sample types as available on suspect cases. Due to the brief viremia associated with JEV infection (4-5 days), there is a limited diagnostic window for virus detection by PCR in blood and serum samples. Further validation may lead to the expansion of the approved sample types in the future.

Epidemiological Investigation and Tracing

Epidemiological investigation and movement tracing during an outbreak are critical in controlling FAD outbreaks. Mosquito surveillance will be included in the epidemiological investigation. While JEV is transmitted through the bite of a mosquito, tracing animal movements may help identify the source of infection and the location of potentially infected animals. This will contribute to defining the extent of the outbreak. Tracing should include consideration of vector habitat and contact of animals with water birds and feral pigs. Tracing efforts for potentially exposed humans will be coordinated with the appropriate public health authority.

Trace-back and trace-forward information should ideally be collected for at least 42 days[29] before the appearance of clinical signs in animals infected with JEV. Additional tracing information will be collected for movements up to the time quarantine was imposed.

[29] 42 days is two times the incubation period listed in the WOAH Terrestrial Code chapter for Japanese Encephalitis.

Tracing

Trace Back: Identifying the origin of all swine and equines that have been brought onto an Infected Premises (IP) in order to establish the original location of their infection.

Trace Forward: The tracing of all swine that have left an IP and could have possibly transmitted infection to, or developed illness on, a new premises. The premises that received the animals should be investigated and kept under surveillance or quarantine.

Forward tracing of dead-end hosts (e.g., equines and cattle) would enable monitoring of their health but is unlikely to contribute to understanding of the epidemiology of the outbreak. Therefore, tracing forward of equids and cattle will not be prioritized.

Quarantine and Movement Control

Preventing contact between JEV and susceptible animals can be partly accomplished through quarantine and movement control. Quarantines and movement controls of swine are critical to contain JE. Infected Premises (IP) should be rapidly quarantined and movement controls should be implemented for swine in the Control Area (CA) until initial risk assessments can be completed. The results of the risk assessments will guide continued need for quarantine and movement controls.

Quarantine is a type of biosecurity protocol that refers to imposing restrictions on entering or leaving a premises, area, or region where disease exists or is suspected. Quarantine stops the movement of infected animals from Infected, Contact, and Suspect Premises.

Movement control refers to activities regulating the movement of animals in an area subject to certain criteria. Movement control is accomplished through a permit system that allows entities to make necessary movements without creating an unacceptable risk of disease spread.

In an FAD outbreak, there may be both State quarantines and Federal quarantines. A response effort begins locally, involving local, State, and Tribal authorities and resources. Each State's animal health emergency response plan should describe the implementation of quarantine and movement controls, including a permit system. If needed, Federal authority and resources will then be employed. USDA may impose a Federal quarantine and restrict interstate commerce from the infected States, asking the States (or adjoining counties) to provide resources to maintain and enforce the quarantine.

All decisions regarding quarantine and movement control will be determined using science-based assessments and will weigh the risk of disease transmission against the need for critical movements and business continuity. Movement controls will be focused on minimizing the spread of infection. Equids do not play a role in transmission and would not be subject to quarantine or movement controls.

Zone, Area, and Premises Designations

Appropriate premises designations will be required for implementation of any quarantine and movement control measures established based on the results of the risk assessments. These designations will be determined in accordance with the *APHIS Foreign Animal Disease Framework: Response Strategies (FAD PReP Manual 2-0)* and *NAEHMS Guidelines: Quarantine and Movement Control*. See Attachment A for further information on zone, area, and premises designations and minimum sizes of zones and areas for JE. Because JEV is spread by a vector, the CA is likely to be at least 30 km (18.6 miles) beyond a known IP. The CA size will be adjusted during the response to consider the range of the endemic mosquito species serving as the vector(s), if such information is available.

Control and Eradication

Eradication strategies are unlikely to eliminate JE because the virus is maintained in mosquito-water bird transmission cycles. Temporary elimination might be possible, but reintroduction would be likely if JEV was already established in an enzootic mosquito-wildlife transmission cycle. Therefore, eradication (i.e., depopulation) is not a part of APHIS' response strategy for JE. The goal will be to manage the outbreak to the extent possible through biosecurity and other control measures or to monitor the disease with limited regulatory intervention.

Horses

Horses, unlike swine, do not maintain sufficient viremia to be epidemiologically important in JEV transmission. If infected horses experience severe illness, including varying degrees of encephalitis and neurological signs, it is possible that they may need to be euthanized for welfare reasons. This decision will be made by the owner and attending veterinarian.

Swine

Swine are amplifying hosts of JEV, posing a risk to humans, horses, and other swine. However, as stated above, the response will focus on control measures, not eradication through depopulation (i.e., stamping out).

Cattle

There is currently no evidence that cattle maintain sufficient viremia to infect mosquitos and therefore are not epidemiologically important in JEV transmission.[30] Although cattle may act as a dead-end host, infection in cattle can result in production losses including loss of appetite and depression. Neurologic signs may follow loss of appetite and depression, making the cattle ineligible for slaughter in the United States.

Vector Control

In the absence of vaccination, the most effective control measures rely on stopping the

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[30] Kuwata, R., Sugiyama, H., Yonemitsu, K., Van Dung, N., Terada, Y., Taniguchi, M., ... & Maeda, K. (2015). Isolation of Japanese encephalitis virus and a novel insect-specific flavivirus from mosquitoes collected in a cowshed in Japan. *Archives of Virology*, 160, 2151-2159.

transmission of JEV by vectors. Vector control will be a critical issue during a JE outbreak and may be immediately instituted upon detection of JE in the United States. The general concept of mosquito control during a JE outbreak is to reduce the mosquito population below transmission thresholds as quickly as possible until the opportunity for JEV transmission is eliminated.

The recommended approach is Integrated Pest Management (IPM) that targets all stages of the mosquito life cycle. This includes adult treatments targeting infected mosquitoes which aims to limit immediate vector transmission and larval treatments to stop future transmission by mosquito vectors. IPM includes field surveys and systematic collections of mosquitoes to optimize resource allocation towards the vector species spreading JEV in a given area. Knowing when the vectors are present during the day or night and their larval habitats allows for targeted use of mitigation strategies.

Space spraying involves treating an open area with an ultralow volume (ULV) or thermal fogging pesticide by hand, truck, or aircraft (including drones). This treatment targets flying or active mosquito vectors that contact the suspended pesticide treatment. Therefore, treatment timing should be when mosquitoes are most likely to be in flight. If sufficient adult mosquitoes are killed this will help stop JEV transmission in the area. However, resting insects will be unaffected by the treatment. A separate larval treatment is needed to kill the aquatic or immature stages that will later emerge as adults and repopulate the area with mosquito vectors.

Various measures to reduce contact with mosquitoes, such as behavioral management include stabling animals in screened barns during peak mosquito biting activity, can be protective, particularly during outbreaks. Environmental management includes reducing mosquito larval habitats by eliminating sources of standing water. Chemical management must be used with caution and in accordance with EPA labels. The EPA maintains resources on integrated mosquito control that can be used during a JE outbreak.

State and local laws and regulations for vector control and insecticide use, including any relevant environmental regulations, must also be considered in any vector control efforts. In addition, personal protection measures should be adhered to when using insecticides of any type.

In the United States, government-level control of insect vectors is primarily left to the discretion of county or municipal governments. APHIS will work closely with CDC, EPA, and local jurisdictions during a JE response in accordance with the *NAHEMS Guidelines: Wildlife Management and Vector Control*.

Vaccination

There is not currently a JE vaccine for swine or horses licensed in the United States. If JE was identified in the United States, APHIS would investigate the current availability of acceptable vaccines, potentially involving emergency approval of vaccines being used in other countries. The USDA has significant regulatory flexibility to respond to emergency conditions related to animal health. Vaccines available worldwide are assessed using a science- and risk-based approach that balances the current animal health situation with the risk of products manufactured outside the U.S. – specifically the risk of foreign animal disease introduction (purity) and to ensure fitness-for-purpose (safety, efficacy against the emergent agent).

Emergency vaccination of swine may be considered to help limit the spread of JEV in the United States according to the "emergency vaccination to live without stamping-out" response strategy outlined in the *APHIS Foreign Animal Disease Framework: Response Strategies (FAD PReP Manual 2-0)*. It may also be used in certain circumstances to limit viral amplification in support of public health (i.e., to reduce human infection).

Vaccination may also be used to limit reproductive losses in swine and to protect horses from developing disease outside of the response activities.

Depopulation, Disposal, and Decontamination

Mass Depopulation and Euthanasia

As stated above, depopulation is not expected to be used as a control strategy.

Disposal

There are no special requirements for disposal of carcasses of animals infected with JEV. The goal is to conduct operations in a timely, safe, bio-secure, aesthetically acceptable, and environmentally responsible manner. Disposal will involve more Federal authorities due to its wider reaching impact on health and the environment. USDA will coordinate with HHS, DHS, and EPA to provide technical assistance and guidance, in alignment with State and local regulations. More information can be found in the *NAHEMS Guidelines: Disposal*.

Cleaning and Disinfection

The goal of cleaning and disinfection (C&D) is to inactivate pathogens at IPs and prevent the off-site spread of pathogens. When performing C&D procedures it is vitally important to do so in the safest and most humane manner as possible. C&D protocols, procedures, and methods, along with safety issues and precautions are more thoroughly discussed in the *NAHEMS Guidelines: Cleaning and Disinfection*.

As noted in Table 1, JEV is susceptible to organic and lipid solvents, common detergents, iodine, phenol iodophors, 70 percent ethanol, 2 percent glutaraldehyde, 3–8 percent formaldehyde, and 1 percent sodium hypochlorite. There are no EPA registered products for use against JEV (as of the writing of this strategy). However, EPA maintains a list of antimicrobial products with claims against common pathogens including emerging viral pathogens.

For JE response, it will also be necessary to consider vector control during the C&D process (e.g., limiting standing water). JEV is unstable in the environment, and most fomites are not implicated in natural transmission of the virus. Non-disposable equipment that is contaminated with blood from potentially viremic animals should be decontaminated to prevent any risk of transmission to people (e.g., through needlestick injury).

Decontamination of equipment and housing on affected pig premises is recommended to prevent transmission via oronasal secretions. On other premises, no decontamination precautions, other than normal hygienic measures, are necessary.

Health, Safety, and Personal Protective Equipment

Because JE is zoonotic and a threat to public health, it is important that appropriate precautions are taken to prevent personnel from contracting JE during a response effort. JEV is most commonly transmitted to humans through the bite of an infected mosquito. Other routes such as inhalation of aerosols or direct contact with contaminated mucus membranes or infective fluids in the laboratory or field setting while collecting tissues samples, are also possible but significantly less likely.

Upon confirmation of JE, public health agencies have the authority and discretion to implement appropriate public health measures. APHIS will work closely with other agencies within USDA, CDC, other federal agencies, state and local public health departments with a One Health approach to protect the safety and health of all personnel and the general population.

One measure to prevent responder exposure to JEV is preventing mosquito bites using repellents and clothing (e.g., long-sleeved shirts and pants). The National Institute for Occupational Safety and Health recommendations for endemic mosquito-borne diseases provide additional guidance for employers and workers which would be applicable during an outbreak of JE. Additionally, APHIS will work closely with CDC and SLTT public health authorities to determine whether vaccination is appropriate for responders and in what circumstances. Personal protective equipment (PPE) is fundamental to ensure personnel are protected from JEV as well as other hazards during a response. This PPE must be appropriately disposed of and/or cleaned and disinfected when leaving an IP.

Responders may also be exposed to other health hazards; prevention of adverse human health events related to emergency response efforts is important. For further information, please see the *NAHEMS Guidelines: Health and Safety* and *NAHEMS Guidelines: Personal Protective Equipment*.

Biosecurity

JEV is not generally transmitted by fomites, but equipment contaminated with blood from viremic animals (e.g., needles, postmortem equipment) may pose a risk to the health of response personnel (e.g., through needlestick injuries). Disposable equipment contaminated with blood should be securely disposed of following existing biosecurity protocols. Reusable equipment contaminated with blood should be decontaminated (see Cleaning and Disinfection). Although there are no additional JE-specific recommendations, general biosecurity measures should be followed according to the *NAHEMS Guidelines: Biosecurity*.

Wildlife Management

Wild birds, such as herons and egrets, which are native to North America, serve as reservoirs for the virus in JEV endemic regions and would likely serve as reservoirs if JEV were introduced into the United States. Additionally, JEV can infect various wild animals, such as mammals, reptiles, and amphibians. It can also infect feral animal populations, such as feral swine and wild horses in the United States.

In the event of a JE outbreak in domestic swine and/or equids, APHIS will work in close collaboration and coordination with other agencies, entities, and units that have primary jurisdiction over wildlife and feral animal populations. Close coordination with wildlife officials will be extremely important as the sylvatic cycle will drive impacts to domestic swine and equids. More details can be found in the *NAHEMS Guidelines: Wildlife Management and Vector Control*.

Communication

A clear and consistent communication strategy is essential for a successful One Health response. APHIS will work with other agencies, including but not limited to CDC, DHS, EPA, and USDA Food Safety Inspection Service (FSIS), to develop synchronized messaging throughout the response. APHIS will communicate with industry and veterinary stakeholders using existing and established communication mechanisms through Veterinary Services. Our communication must be early, accurate, and transparent to build public trust. We will develop communication materials for the media, public, swine and horse owners/producers, and veterinarians.

APHIS has developed key initial messages for the response. Further messaging and communication products will be developed in coordination with our partners and tailored to the specifics of the outbreak. Appendix B includes example fact sheets intended for swine producers and equine stakeholders.

Key Initial Messages

- Japanese encephalitis virus (JEV) is not a food safety concern. Pork meat and pork products are safe to eat.
- JEV virus is transmitted to humans through the bite of an infected mosquito. It does not spread from person to person. Animals like pigs and horses cannot directly pass the virus to people.
- JEV can infect horses, mules, donkeys, and pigs. If you raise pigs, you should look for signs of illness and report any unexplained abortions or stillbirths to your veterinarian.
- People who work with pigs and horses, even if they are only backyard pets or a small herd, should take steps to control mosquitoes and continue to practice good biosecurity.
- USDA and CDC are working closely with their State, local, Tribal, and territorial public health partners to ensure a coordinated response.

Because the mosquitoes that transmit WNV are likely the same mosquitoes that would transmit JEV in the United States, many of the public education strategies outlined in the CDC's "West Nile Virus in the United States: Guidelines for Surveillance, Prevention, and Control" could be adapted to communicate with the public and livestock producers during a JE outbreak. APHIS will work with the CDC to coordinate this messaging.

Table A-3. Sample Minimum Sizes of Zones and Areas for Mosquito or Culicoides Vector-Borne Diseases

Note: This table is a baseline as outlined in the NAEHMS Guidelines: Quarantine and Movement Control. During the response, many factors which affect mosquito flight activities (such as wind and nearby land use) and the mosquito species in an area will be used to establish these zones. Perimeters may be larger or smaller than those listed below.

Zone or area	Minimum size and details
Infected Zone (IZ)	Perimeter should be at least 10 km (~6.2 miles) beyond perimeters of presumptive or confirmed Infected Premises. Will depend on disease agent and epidemiological circumstances. This zone may be redefined as the outbreak continues.
Buffer Zone (BZ)	Perimeter should be at least 20 km (~12.4 miles) beyond the perimeter of the Infected Zone. Width is generally not less than the minimum radius of the associated Infected Zone but may be much larger. This zone may be redefined as the outbreak continues.
Control Area (CA)	Perimeter should be at least 30 km (~18.6 miles) beyond the perimeter of the closest Infected Premises. Please see Table 3-1 in FAD PReP Manual 2-0 for factors to consider in determining the size of a Control Area. This area may be redefined as the outbreak continues.
Surveillance Zone (SZ)	Width should be at least 20 km (~12.4 miles) but may be larger depending on the known geographic range of vector.

How can I minimize the risk of JEV to my pigs?

Is there a vaccine?

There is currently not a vaccine available in the United States.

Control mosquitoes on your property

Monitoring for mosquitoes at the various stages of their lifecycle helps to determine the most effective control methods. Key measures that will help reduce mosquito numbers on your property include:

- Inspecting bodies of water and containers for larvae, as well as areas where adult mosquitoes rest, like ceilings and walls
- Removing anything in the open that is filled with water or has the potential to hold water
- Filling in potholes or other areas that collect water
- Clearing debris from gutters, downspouts, and drains around buildings so that water doesn't pool
- Trimming overhanging tree branches where mosquitoes may rest
- Ensuring effluent drainage is free flowing, flushed regularly and does not pool
- Sealing tanks, wells or other large water containers, or screening with 1mm mesh
- Installing insect screens
- Using fans inside buildings where pigs are housed to disrupt mosquito activity

What do I do if I suspect my pigs have JE?

JE is a notifiable disease in the United States.

If you suspect JE (or any other notifiable disease) in your pigs, please call your private veterinarian or State Animal Health Official.

How does JEV affect people?

Humans can also be infected with JEV. Most infections in people cause no symptoms. Some people experience a fever and headache, but severe cases may result in convulsions, disorientation, and coma. If you experience any worrisome symptoms, you should seek medical advice from a healthcare provider immediately.

You can protect yourself by preventing mosquito bites.

- Use 5HSHOOHQWV3URWHFWLRQDJDLQVW0RVTXLWRHV7LFNVDQG2WKHU$WKURSRGV_86(3
- Wear loose-fitting long-sleeved shirts and pants when outdoors, especially between dawn and dusk

Additional resources

Reach out to your local University extension services, local environmental/mosquito control agency, and/or your veterinarian for additional assistance.

Swine Health Information Center JEV Fact Sheet
Centers for Disease Control and Prevention JEV Website
Environmental Protection Agency Mosquito Control Website