

EXOTIC

Japanese encephalitis

Fact sheet

Introductory statement

Japanese encephalitis (JE) is the principal cause of epidemic viral encephalitis in humans and horses in many parts of Asia. It appears to be extending its range, most significantly towards the Torres Strait and other islands bordering Australia. JE is presently exotic to Australia but is considered a significant threat because the host species and at least two competent vectors are present, and it entered the Australian mainland once in 1998. Movements of wild birds and local human populations (with possible associated introduction of vectors or pigs) in the north pose a risk for introduction. Feral pigs in Australia are an abundant and widespread potential wildlife reservoir. JE can infect a wide range of species and it is uncertain if other Australian fauna could be reservoirs or clinically affected by JE. However, recent work suggests that flying foxes could play a role in the dispersal of Japanese encephalitis virus (JEV) in Australia.

Aetiology

Virus: Japanese encephalitis virus (JEV); Genus: *Flavivirus*; Family: *Flaviviridae*

NB: Other notable viruses in this genus include Murray Valley encephalitis, Kunjin, Dengue, West Nile and St Louis encephalitis viruses

Grouping (non-taxonomic): Arbovirus (**Ar**thropod **borne virus**, see separate factsheet on Arboviruses for more details).

Natural hosts

Primary host: Birds, especially herons and egrets (van den Hurk et al. 2009a)

Amplifying host: Pigs and wild birds (van den Hurk et al. 2009a)

Other clinically affected hosts: Horses, donkeys and humans (dead-end hosts; >95% of human infections are asymptomatic; Hills et al. 2015)

Other clinically unaffected hosts: Cattle, sheep, goats, dogs, cats, rodents, bats, reptiles and amphibians (roles uncertain).

World distribution

JEV occurs in temperate and tropical regions of eastern and southern Asia: Bangladesh, Bhutan, India, Myanmar, Nepal, Sri Lanka, China, Japan, Korea, maritime Siberia, Taiwan, the Philippines, Vietnam, Cambodia, Indonesia, Laos, Malaysia, Thailand, Papua New Guinea, the Torres Strait islands, and potentially Pakistan (Geering et al. 1995).

The range of JE is considered to be expanding. Major epidemics have occurred when the virus spread into new areas, e.g. India in the late 70s (Geering et al. 1995). In the Torres Strait, JEV has been isolated from humans and pigs and other animals have tested serologically positive. One confirmed human case occurred on the Australian mainland (Cape York Peninsula) in 1998 (van den Hurk et al. 2009a) and JEV was isolated from a mosquito, also on Cape York Peninsular, in 2004 (van den Hurk et al. 2009a). Strong winds, such as those associated with cyclones, are suspected to be capable of blowing infected mosquitoes from Papua New Guinea into Northern Australia (Hanna et al. 1999).

Occurrences in Australia

JE is considered exotic to Australia but sporadic cases have been reported: in 1995 three human cases, two of which were fatal) occurred on Badu Island in the Torres Strait (van den Hurk et al. 2006), in 1998 another case was reported from Badu Island (Australian Department of Health and Ageing 2004), and one week later a fisherman contracted JE in the Mitchell River area on the western side of Cape York Peninsula (Ritchie and Rochester 2001). The latter case is the only known human case from the Australian mainland. Seroconversion has also been documented in sentinel pigs on Cape York Peninsula (Australian Department of Health and Ageing 2004). In 2004, JEV was isolated from a mosquito, also on the Cape York Peninsula (Hanna et al. 1996). However, there is no evidence to suggest JEV has established on mainland Australia, likely due to mosquitoes preferring to feed on macropods rather than pigs (Hanna et al. 1999).

Epidemiology

Transmission

JEV is transmitted via the bite of a competent mosquito vector and it has been isolated from more than 30 mosquito species. Certain insectivorous animals (e.g. lizards and bats) may also contract the virus after ingesting infected mosquitoes. In addition, transmission of the virus via semen from infected boars is also possible (Hanna et al. 1999). It is uncertain if transmission via infected milk is possible (Hanna et al. 1999; van den Hurk et al. 2006). Wild birds act as reservoirs and pigs act as amplifying hosts for JEV (van den Hurk et al. 2006). Horses, humans and ruminants are considered to be dead-end hosts. It is uncertain if other affected species or Australian native fauna may be reservoirs for this virus (Hanna et al. 1999; van den Hurk et al. 2003).

Transmission generally occurs in agricultural zones, particularly in the vicinity of pig farms and irrigated areas such as rice paddies. *Culex tritaeniorhynchus* is the primary vector of JEV and thrives in the rice paddies of South East Asia where wading birds also flourish, thus completing the life cycle (Animal Health Australia 1998). Within Australia *Cx. annulirostris* is considered the likely primary vector, though *Cx. gelidus* and *Cx. palpalis* are also competent vectors (Animal Health Australia 1998). Research on mosquito feeding patterns in

Australia indicates that marsupials, particularly the agile wallaby (*Macropus agilis*), are preferred to feral pigs and birds (van den Hurk et al. 2009a). As marsupials are thought to be inefficient hosts for the transmission of JE, preferential feeding by vectors may impede the establishment of JE in Australia (Animal Health Australia 1998).

A recent study showed transmission of JEV from the black flying-fox, *Pteropus alecto*, to *Cx. annulirostris* mosquitoes, despite the absence of detectable viraemia (Halstead and Jacobson 2003). To determine the potential role of flying-foxes in transmission cycles of JEV in Australia, the authors exposed *P. alecto* to JEV via infected *Cx. annulirostris* mosquitoes or inoculation. No flying-foxes developed symptoms consistent with JEV infection. Anti-JEV IgG antibodies developed in 6/10 flying-foxes exposed to infected *Cx. annulirostris* and in 5/5 inoculated flying-foxes. Low-level viraemia was detected by real-time reverse transcriptase polymerase chain reaction in 1/5 inoculated flying-foxes, and this animal was able to infect recipient mosquitoes. Although viraemia was not detected in any of the 10 flying-foxes that were exposed to JEV by mosquito bite, two animals infected recipient mosquitoes. Likewise, an inoculated flying-fox without detectable viraemia infected recipient mosquitoes. Although infection rates in recipient mosquitoes were low, it was concluded that the high population densities in roosting camps, coupled with migratory behaviour indicate that flying-foxes could play a role in the dispersal of JEV (van den Hurk et al. 2009a; Hall-Mendelin et al. 2012).

Morbidity rate

- Humans: Less than 1% (van den Hurk et al. 2003; Hall-Mendelin et al. 2012).
- Pigs: 0-70%
- Horses: 0.04-1.4%

Mortality rate in symptomatic cases

- Humans: 25%
- Pigs: 0% (Adult pigs), 5.4-35% (foetal pigs)
- Horses: 5% up to 30-40% in outbreaks (van den Hurk et al. 2003)

Incubation period

- Humans: 6-16 days
- Pigs: 1 day
- Horses: 8-10 days
- Herons: 1-2 days (van den Hurk et al. 2009b)
- Bats, reptiles and amphibians: extended incubation possible; experimental studies demonstrated viraemia in bats after 107 days of artificial incubation. These studies considered the main overwintering mechanism of JEV in Japan to be reintroduction by wild birds, and extended incubations in amphibians, reptiles and bats (van den Hurk et al. 2009b).

Clinical signs

Humans: Acute signs in humans include sudden onset of fever, gastrointestinal signs and headache. 20-50% may develop encephalitis with associated neurological signs. Approximately 30% of survivors are left with ongoing and normally severe sequelae (Hills et al. 2015)..

Pigs: Transplacental transmission of JEV can cause foetal encephalitis, abortion and stillbirth, with mummified foetuses. JEV can cause poor fertility in boars. Non-pregnant animals may show no signs. Surviving piglets commonly exhibit tremors, convulsions and death. Encephalitis may occur in piglets up to six months of age (see Animal Health Australia 1998).

Horses: Three clinical syndromes (see Animal Health Australia 1998):

1. Transient syndrome: fever up to 40°C for 2-3 days with anorexia, sluggish movement and congested or jaundiced mucous membranes; followed by an uneventful recovery
2. Lethargic syndrome: the above signs plus fevers reaching 41°C for up to a week, difficulty in swallowing, neck rigidity, radial paralysis, pronounced lethargy and falling or staggering
3. Hyperexcitable syndrome: high fever, aimless wandering or violent demented behaviour, blindness, profuse sweating, trembling, collapse and death.

Diagnosis

In humans and animals, JE is confirmed either by isolation of the virus or by a rising antibody titre (in the absence of recent vaccination). In animals, a serum neutralisation test or immunohistochemistry may also confirm the diagnosis (van den Hurk et al. 2009a). If, in humans, the infection is believed to be acquired in Australia, confirmation from a second reference laboratory is required.

Clinical pathology

In humans, clinical laboratory findings of JE include moderate leucocytosis, mild anaemia, hyponatraemia, and cerebrospinal fluid (CSF) pleocytosis with a lymphocytic predominance (Animal Health Australia 1998; Hills et al. 2015).

Pathology

There are no characteristic gross lesions in humans, animals or aborted fetuses. Oedema of the brain may be present in piglets.

In animals: histologically, there may be pronounced necrosis of Purkinje cells in the cerebellum with no inclusion bodies. A diffuse non-suppurative encephalomyelitis with neuronal necrosis, neuronophagia, gliosis, perivascular cuffing, spinal hypomyelination and engorged blood vessels with many mononuclear cells may be seen. Similar changes may be seen in humans.

Differential diagnoses

Pigs

Diseases which cause abortions in sows and neurological diseases in piglets should be considered as differentials, e.g. Aujeszky's disease, blue eye paramyxovirus, classical swine fever, haemagglutinating encephalomyelitis, Leptospirosis, porcine brucellosis, porcine polioencephalomyelitis (either Talfan or Teschen type), porcine parvovirus, porcine Reproductive and Respiratory Disease, Salmonellosis and salt poisoning (Animal Health Australia 1998).

Horses

Diseases which cause fevers and neurological symptoms or ataxia in horses should be considered as differentials.

Laboratory diagnostic specimens

In animals, diagnosis is made from serum, or from brain and other tissues collected aseptically and less than 12 hours post-mortem from animals in the acute stage of the disease. A range of fixed tissue samples should also be collected. Fresh samples should be transported chilled to the local government diagnostic laboratory, if expected to arrive within 48 hours after collection. Otherwise samples should be frozen and transported on dry ice (Hills et al. 2015).

Laboratory procedures

Virus isolation may be performed in appropriate cell line cultures after mouse inoculation with clinical material. Serological tests used in both animals and humans include complement fixation, haemagglutination inhibition, serum neutralisation and/or enzyme-linked immunosorbent assay. Additional tests used in humans include immunoglobulin detection in serum or CSF, and detection of JEV RNA in clinical material (Table 1) (Animal Health Australia 1998).

Treatment

There is no treatment for JEV infection. For humans, symptomatic and supportive treatment may be appropriate depending on clinical signs.

Table 1. Summary of test rationale, specimens required and time delay for the various tests available for JE in animals. (C-ELISA – Competitive enzyme linked immunosorbent assay, MVE – Murray Valley Encephalitis Virus, KUN – Kunjin Virus, CNS – Central nervous system)

Tests for animals	Specimen required	Test rationale	Time taken (days)
Non-lethal tests			
Flavivirus C-ELISA	Serum	Rapid Non-specific	1
JE, MVE and KUN specific C-ELISAs, as a panel	Serum	Quick Although detects specific antibody, may be unreliable	2
Serum neutralisation test	Serum	Most specific, confirmatory Slower	7
Post-mortem tests			
Histopathology	Formalin fixed or fresh tissue (esp. CNS or aborted fetuses)	Quick Suggestive microscopic changes, but not definitive	2
Immunohistochemistry	Formalin fixed or fresh tissue (esp. CNS or porcine fetuses)	Confirms histopathological suspicions	3
Virus isolation and identification	Whole blood, CNS tissue	Confirmatory Delayed result	14-21

Prevention and control

Where possible, animals suspected of being infected should be isolated (with adequate insect-proof housing and control) and observed. There should be restricted movements of at-risk domestic pigs (within a Control Area adjacent to all infected premises or areas of known viral activity). Horses should be treated with

Ivermectin to disrupt transmission of the virus and lower the likelihood of infections (Animal Health Australia 1998).

In humans, pigs and horses, vaccination is a possible control method but there are limitations and considerations with deployment, side-effects and supplies (Animal Health Australia 1998). Mosquito-bite prevention should be exercised in both animals and humans. Ongoing or targeted mosquito control should also be performed, as appropriate. Piggeries should be located a minimum of 3 km from human dwellings.

No special precautions are recommended for handling of animal carcasses or pathological specimens. Milk and semen from infected animals should not be used (Animal Health Australia 1998).

Surveillance and management

The AUSVETPLAN for JE is available at:

<https://www.animalhealthaustralia.com.au/our-publications/ausvetplan-manuals-and-documents/>.

Vaccination may be considered as an eradication strategy.

In Australia, JE is a notifiable disease in both humans and animals. Trace-back activities may be instigated on infected humans and animals, and pigs may be monitored for further viral activity. Serum banking of potential wild animal hosts for later testing may be helpful (Animal Health Australia 1998).

Japanese encephalitis (JE) virus surveillance is conducted during the wet season in northern Queensland. there has been no evidence of JEV circulation on the mainland since early 2004 (Animal Health Australia 1998, 2015).

Statistics

Wildlife disease surveillance in Australia is coordinated by the Wildlife Health Australia. The National Wildlife Health Information System (eWHIS) captures information from a variety of sources including Australian government agencies, zoo and wildlife parks, wildlife carers, universities and members of the public. Coordinators in each of Australia's States and Territories report monthly on significant wildlife cases identified in their jurisdictions. NOTE: access to information contained within the National Wildlife Health Information System dataset is by application. Please contact admin@wildlifehealthaustralia.com.au.

There are no reports of JE in Australian wildlife in the National Wildlife Health Surveillance Database (at 3 March 2016).

Research

AUSVETPLAN recommends that the National Arbovirus Monitoring Program and flavivirus sentinel programs should monitor the spread of JE through the use of appropriate sentinel hosts and vector testing and monitoring (Animal Health Australia 1998).

To fully evaluate the potential impact of JE in Australia it is necessary to:

- Evaluate Australian fauna as potential reservoirs or clinically affected species.
- Conduct epidemiological modelling of spread of JE in Australia based on vector competence, abundance and movement and potential host dynamics (including wild birds and feral pigs).
- Conduct in-depth testing of biosecurity measures currently in place.

- Evaluate the significance of time delays between detection, reporting and control measures.
- Conduct financial impact analyses of a JE incursion or establishment as an endemic disease.

Human health implications

JEV is responsible for more than 40,000 human cases of clinical JE each year, with an expected case fatality ratio of around 25% (Animal Health Australia 1998, 2015) and up to 50% of affected humans have serious sequelae (Animal Health Australia 1998). Most infections occur in small clusters at the end of the mosquito breeding season or summer (Hanna et al. 1999; Animal Health Australia 2015).

The Australian Department of Health has state-specific fact sheets on Australian arboviruses, including JE, that should be consulted for further information on JE and human health (see:

<http://www.health.gov.au/internet/main/publishing.nsf/Content/health-arbovirus-resources-factsheets.htm>).

Conclusions

JE is exotic to Australia. It may cause severe clinical disease in humans and horses, and abortion and stillbirths in pigs. JE was identified as being a major threat to the Australian pig industry, ranking second only to rabies in overall threat posed (Animal Health Australia 1998). The range of JEV is extending in neighbouring Asian countries and into the Torres Strait islands. It has entered the Australian mainland via wild bird, pig or vector movements but is not currently established in Australia. Wildlife reservoirs such as feral pigs and birds together with competent vectors within Australia contribute to the risk of its establishment. The primary mosquito vector (*Cx. annulirostris*) for JEV in Australia feeds mostly on marsupial blood, particularly from the agile wallaby, a poor amplifying host for the virus. Consequently, feeding preferences of *Cx. annulirostris* may be precluding JEV establishment on the Australian mainland. It is uncertain whether other Australian fauna such as dingos, marsupials, bats, amphibians and reptiles are susceptible, are potential reservoir hosts, or may play a role in impeding the establishment of JE because of mosquito feeding preferences. However, recent work suggests that flying foxes could play a role in the dispersal of JEV in Australia.

References and other information

Animal Health Australia (1998) Australian Veterinary Emergency Plan. AUSVETPLAN. Disease Strategy. Japanese Encephalitis. *AUSVETPLAN Edition 2.0* Available at <http://www.animalhealthaustralia.com.au/wp-content/uploads/2011/04/jedfinal.pdf> [Accessed 15 April 2015].

Animal Health Australia (2015) Animal Health in Australia 2014. Animal Health Australia, Canberra, ACT.

Australian Department of Health and Ageing (2004) 'Japanese encephalitis fact sheet.' Available at <http://www.health.gov.au/internet/main/publishing.nsf/Content/health-arbovirus-pdf-fsjapanese.htm> [Accessed 09/07/2009].

Geering, W, Forman, A, Nunn, M (1995) 'Exotic Diseases of Animals: a field guide for Australian veterinarians.' (Australian Government Publishing Service: Canberra).

Hall-Mendelin, S, Jansen, CC, Cheah, WY, Montgomery, BI, Hall, RA, Ritchie, SA, van den Hurk, AF (2012) *Culex annulirostris* (Diptera: Culicidae) host feeding patterns and Japanese Encephalitis Virus ecology in Northern Australia. *Journal of Medical Entomology* **49**, 371-377.

Halstead, SB, Jacobson, J (2003) Japanese Encephalitis. *Advances in Virus Research* **61**, 103-138.

Hanna, JN, Ritchie, SA, Phillips, DA, Lee, JM, Hills, SL, van den Hurk, AF, Pyke, AT, Johansen, CA, Machenzie, JS (1999) Japanese Encephalitis in North Queensland, Australia, 1998. *Medical Journal of Australia* **170**, 533-536.

Hanna, JN, Ritchie, SA, Phillips, DA, Shield, J, Bailey, MC, Machenzie, JS, Poidinger, M, McCall, BJ, Mills, PJ (1996) An outbreak of Japanese Encephalitis in the Torres Strait, Australia, 1995. *Medical Journal of Australia* **165**, 256-260.

Hills, SL, Rabe, IB, Fischer, M (2015) Japanese Encephalitis. In 'Yellow Book - Chapter 3 - Infectious Diseases Related to Travel.' (Centers for Disease Control and Prevention Available at <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/japanese-encephalitis> [Accessed 28 February 2016].

Ritchie, SA, Rochester, W (2001) Wind-blown mosquitoes and introduction of Japanese Encephalitis into Australia. *Emerging Infectious Diseases* **7**, 900-903.

van den Hurk, AF, Johansen, CA, Zborowski, P, Paru, R, Foley, PN, Beebe, NW, Machenzie, JS, Ritchie, SA (2003) Mosquito host-feeding patterns and implications for Japanese Encephalitis Virus transmission in northern Australia and Papua New Guinea. *Medical and Veterinary Entomology* **17**, 403-411.

van den Hurk, AF, Montgomery, BI, Northill, JA, Smith, IL, Zborowski, P, Ritchie, SA, Machenzie, JS, Smith, GA (2006) Short report: The first isolation of Japanese Encephalitis virus from mosquitoes collected from mainland Australia. *American Journal of Tropical Medicine and Hygiene* **75**, 21-25.

van den Hurk, AF, Ritchie, SA, Mackenzie, JS (2009a) Ecology and geographical expansion of Japanese Encephalitis Virus. *Annual Review of Entomology* **54**, 17-35.

van den Hurk, AF, Smith, CS, Field, HE, Smith, IL, Northill, JA, Taylor, CT, Jansen, CC, Smith, GA, Mackenzie, JS (2009b) Transmission of Japanese Encephalitis Virus from the Black Flying Fox, *Pteropus alecto*, to *Culex annulirostris* mosquitoes, despite the absence of detectable viremia. *American Journal of Tropical Medicine and Hygiene* **81**, 457-462.

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To provide feedback on this fact sheet

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