Japanese encephalitis emergence in Australia: the potential population at risk

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FiAbstract:

In Australia, Japanese encephalitis virus circulated in tropical north Queensland between 1995 and 2005. In 2022, a dramatic range expansion across the southern states has resulted in 30 confirmed human cases and six deaths. We discuss the outbreak drivers and estimate the potential size of the human population at risk.

Keywords. Japanese encephalitis, emerging diseases, zoonoses, transmission pathways.

1. BACKGROUND

Japanese encephalitis virus (JEV) is a single-stranded RNA flavivirus transmitted by mosquitoes of the genus *Culex*. Amplifying hosts include wading birds and swine. Most mammals, including humans, do not amplify the virus to the degree needed to infect mosquitoes and facilitate onward transmission. In endemic countries, a small proportion (<1%) of infected people exhibit symptoms, ranging from non-specific febrile illness to severe encephalitis with convulsions [1]. In regions with no immunity, the proportion of overt infections may be far higher [2]. The fatality rate among symptomatic cases is around 30% with half of survivors experiencing cognitive or neurophysiological sequelae [1].

Japanese encephalitis is a vaccine-preventable disease, but the leading cause of viral encephalitis in Asia, with an estimated 68 000 cases per year [3]. Until 2022, the southerly limit of the disease was the far north of Australia where, in 1995, there were three cases and two deaths on Badu Island [4], and a further two cases from that island and Cape York in 1998 (one recovered, one with ongoing cognitive challenges) [5]. An additional death from JEV in the Tiwi Islands, Northern Territory (NT) occurred in 2021 [1]. In north Queensland (QLD), JEV was recovered annually from mosquitoes and/or domestic pigs in 1995-1998, and 2000-2005. JEV surveillance in QLD was then scaled back [6] and subsequent, limited mosquito screening yielded no further detections. In 2020 however, Queensland Health reported the seroconversion of domestic pigs to JEV in Cape York [7].

2. THE CURRENT OUTBREAK

On February 25th 2022, JEV was isolated from a commercial pig farm in southern QLD following investigation of high abortion and stillbirth rates in farrowing sows. Notifications from piggeries in New South Wales (NSW), Victoria (VIC) and South Australia (SA) followed [8]. Sampling of piggeries occurred in response to symptoms. The presence of JEV was determined by PCR detection in foetuses although identification of JEV specific IgM was also used. National reference laboratories provided verification [8].

As of August 25th 2022, 40 human JE cases have been reported by the Australian Department of Health including 30 confirmed (six dead) and 10 probable. Case definitions are set by the Communicable Disease Network of Australia (Supplementary data, Table S1a). Their criteria for laboratory confirmation include the unequivocal detection of virus by nucleic acid amplification or isolation. However, most human cases are identified by serological tests [9] which have issues of sensitivity, and cross-reactivity with endemic flaviviruses such as

Kunjin [WNV_{KUN}] and Murray Valley Encephalitis Virus [MVEV]. These must be ruled out in order to confirm a JE case. Testing for JEV-specific IgM in cerebrospinal fluid (CSF) has high sensitivity and specificity but assays conducted on JEV-specific IgG in CSF or serum must compare acute and convalescent sera and demonstrate four-fold or greater increases in titre. The "gold-standard" for those assays are neutralisation tests [9]. JE case identification is confirmed by a public health reference laboratory (Table S1a).

The JEV genotype causing the current outbreak is genotype IV [9]. This is associated with the 2021 human case from the Tiwi Islands. It is not the genotype isolated during the 1995 and 1998 Australian outbreaks (I, II).

A variety of factors may have caused the recent expansion of JEV in Australia. Firstly, 2021 / 2022 were La Niña years, causing extraordinarily high rainfall during typical Australian summer temperatures (Figure S2). In temperate Australia, La Niña is also associated with outbreaks of the similar zoonotic, mosquito-borne MVEV [10]. This climate system created new temporary wetlands across southern Australia which may have impacted the movement and distribution of JEV-infected wading birds dispersing from the north. It also created optimal habitats for the proliferation of *Culex annulirostris* which was the key JEV vector in north QLD and is abundant across mainland Australia [6].

Where new wetlands, viraemic birds and high mosquito densities converged near piggeries, the probability of "spill over" and rapid amplification in domestic pigs increased. Infected piggeries may then have become a source of virus for vector-borne transmission to humans. However, other pathways involving feral pigs or wild birds may also sustain JEV infection. In Australia, the geographic spread of JEV in 2022 may have been aided by intensive pig farming and a large feral pig population [1, 6]. Oronasal transmission among domestic pigs presents an additional infection route [11] while JEV exposure in feral pigs was reported from northern Australia in 2022 (Table S1b).

An effective JEV vector is one that is highly competent at the viral titres encountered in the serum of viraemic birds or swine. In order to facilitate transmission to humans, these vectors must display a biting preference for those amplifying hosts and humans. Mosquitoes must also occur at sufficient densities to ensure that a proportion live long enough to feed on an infected host, incubate the virus, and disseminate the infection to their salivary glands.

Culex annulirostris is considered the major Australian vector of JEV, although the relative competence of different lineages of that species remains unknown [12]. It feeds opportunistically on a variety of vertebrates, proliferates under optimal conditions and is capable of dispersing > 4 km per day (Table S3). Other endemic mosquito species that may play a role include two recently established vectors with limited distributions. *Culex gelidus* has been implicated in previous Australian JEV outbreaks, while *Cx. tritaeniorhynchus* is responsible for the majority of JE transmission in Asia (Table S3).

Currently, none of the human cases reported appear to be associated with an occupational hazard (Table S1a**)**. This suggests that it is the dispersal capacity of the mosquito, rather than the occupation of the infected human, that dictates the current risk. This presents a quandary for Australia's health authorities, who are battling with limited vaccine supplies and the identification of at-risk groups.

3. ESTIMATING THE HUMAN POPULATION AT RISK

Currently, Australian health departments have not released the locations of human JEV cases but the locations of many infected piggeries and humans have been detailed by the World Organisation for Animal Health [8], and by local media organisations. The precise or approximate locations of > 50 JE exposed piggeries (24 from NSW, 6 from QLD, 6 from South Australia and 17 from VIC) (Table S1c) and 22 locations associated with human infections (10 from NSW, 2 from QLD, 7 from SA, 2 from VIC, and 1 from the Northern Territory (NT)) are available (Table S1a). Although the majority of reports congregate around the NSW / VIC border, the perimeter of the current JEV outbreak now contains 600,000 km^2 of eastern and southern Australia, on both sides of the Great Dividing Range (Figure 1A).

The well-characterised JEV vector, *Cx. annulirostris*, can disperse a considerable distance (4.4 km, Table S3). Our aim was to identify the human population within this distance of a piggery and therefore potentially at risk of infection. There is no complete database of all piggery locations available in the public domain, but we downloaded locations from the Farm Transparency Project (https://farmtransparency.org). Some of the piggery locations noted in Table S1c were not listed by that project so both datasets (n = 699) were combined and mapped to create Figure 1A.

To estimate the population at risk of being bitten by an infected mosquito dispersing from a piggery (Figure 1B), we downloaded raster data for the Australian human population (resolution of 100 m) updated to 2020 by WorldPop [https://www.worldpop.org]. The Python code for linking (‘masking’) the boundaries of various radii around known piggery locations to the human population raster is available on github [https://github.com/lwyakob/JEV].

Our illustrative maps and analyses have major limitations that include an approximation of human case locations, an assumption that all piggeries are equally susceptible to infection and a poor understanding of true dispersal behaviours of the vector. Nonetheless, if we assume that all mapped piggeries are vulnerable to infection, and that infected vectors fly 4.4 km over their lifetimes (i.e., *Cx. annulirostris*; Table S3), then 740,546 people are potentially at risk of receiving an infective bite (Figure 1B).

4. CONCLUSIONS

This initial analysis demonstrates that around 3% of the human population in Australia may be vulnerable to JEV infection following its recent range expansion, if piggeries are a major source of virus. Figure 1A suggests that JEV is now endemic over a large part of sub-tropical and temperate Australia. This winter, as temperatures declined and floodwaters receded, the virus may have retreated into the wild reservoir. This is the pattern for MVEV which is also maintained in wading birds and spills over into the human population during La Niña years [10]. The interval until the next JEV outbreak is impossible to predict but a warming climate and extreme flood events may exacerbate transmission and increase the frequency and severity of outbreaks.

In the future, protection from JEV in Australia may require: 1) intensive surveillance of piggeries, 2) targeted vaccination of humans, 3) an understanding of virus movement from northern Australia and Asia, 4) studies on the vectorial capacity of mosquitoes for invading JEV genotypes, and 5) characterization of the epidemiological role of wading birds and feral pigs.

NOTES

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7. FUNDING

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8. **CONFLICTS OF INTEREST**

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. No conflicts of interest have been identified

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Figure 1. The current distribution of JEV in Australia, and the human population at risk. **A**. The distribution of piggeries (pink circles), the locations of JEV exposed or infected piggeries (red circles), and places associated with human JEV cases (blue triangles) in 2022. The map also shows JEV distribution in relation to elevation and the presence of the Great Dividing Range (shaded grey). **B.** The human population at risk, assuming that all piggeries can be infected and that mosquitoes have considerable dispersal potential (code: https://github.com/lwyakob/JEV).

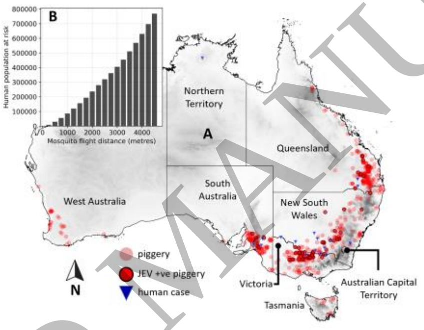

Figure 1
60x45 mm (x DPI)