Japanese encephalitis in northern Australia

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Geographic range of Japanese encephalitis virus
Japanese Encephalitis

The major cause of childhood viral neurological infection and disability in Asia.

- Most cases are asymptomatic, with 1:30-1:300 case:infectivity rates;
- Clinical disease is encephalitis (75-85%), meningitis (5-10%), myelitis (5-10%)
- Of clinical cases, ~25% fatal, 50% have severe-psychiatric sequelae, and 25% fully resolve;
- Most cases occur in young children in endemic areas;
- Insufficient knowledge of disease burden in most regional countries;
- JE is a zoonosis, normally circulating between mosquitoes and pigs or waterbirds (particularly ardeid birds).
- About 45,000 cases reported annually in Asia, but this may be a gross under-reporting, with some estimates of over 175,000 cases annually.
JE MOVEMENT

- It has long been recognised that JE virus has a high propensity to move into and colonise new areas.
- This has often been due to the development of new rice paddy fields, often associated with land clearing, deforestation, and changed agricultural practices.
- Most recent expansion has been into Haryana State, India (1993); Pakistan (1994), Torres Strait (1995), Kerala State, India (1996), Cape York, Australia (1998).
Weaver and Reisen, 2010
MOZZIE VIRUS KILLS BOY, 16
JEV in Northern Australia – 1
Incursion due to Topotype 2 JEV

1995: JEV first described in islands of the Torres Strait of northern Australia, with three human cases and two deaths. Initially thought to be Murray valley encephalitis. – At the time, the closest known JE virus had been isolated in Indonesia, on Flores, and the closest case had been on Bali – 3000km to the west!

The outbreak was widespread in the Torres Strait - 58/1046 sera from inhabitants of 4 islands in the north and central Torres Strait were antibody-positive for JE virus; and 97/115 pig sera from 9 islands were antibody-positive for JE virus.

1995-96: Residents of the Torres Strait islands were offered JE vaccine (Biken, mouse brain-derived), and almost all were immunised.

1996-97: JEV activity was again observed in sentinel pigs;.
JEV in Northern Australia – 2
Incursion of topotype 2 virus

1998: JEV occurred again in the Torres Strait, with another human case on Badu Island and the first human case on mainland Australia. Viruses were also isolated from mosquitoes and pigs, and serological data demonstrated that a number of pigs had been infected in both the Torres Strait and the mainland.

The JEV isolates were all virtually identical and belonged to topotype 2.

A major feature of the outbreak was the close association between pigs and humans, and the mosquito breeding sites.
JEV in the Torres Strait and Northern Australia

1995

1998
Host feeding patterns of *Cx. annulirostris* on Badu Island 1996-1998

- Pig: 41.25%
- Horse: 31.25%
- Dog: 11.25%
- Human: 6.25%
- Bird: 1.25%
- Cat: 3.75%
JE virus in Papua New Guinea

- Retrospective serological evidence showed that human JE virus infections had occurred in southern PNG since 1989, particularly in Western Province.
- We isolated JEV from mosquitoes in 1997 and 1998 at three sites in Western Province, and the virus was shown to be identical to the isolates from the Torres Strait.
- Four cases of JE infection were recognised at Rumginae Hospital, near Kiunga, Western Province, in 1997/1998, 2 of which were fatal.
- JEV spread to domestic pigs in 1998 in northern PNG, and in humans in Milne Bay Province, late 1997 and 1998.
- Evidence suggests that JEV is now endemic in PNG and West Papu, and was almost certainly the source of virus emerging in the Torres Strait.
HUMAN CASES OF JAPANESE ENCEPHALITIS FROM PAPUA NEW GUINEA

(All cases from Rumguinea Hospital, near Kiunga, Western Province)

Case 1: 4-year-old girl from Ipoknai Village, near Kiunga. August 1997. Symptoms of fever, neck stiffness, convulsions, coma. Recovered with minor sequelae (impaired speech)

Case 2: 12-year-old girl from Rokonda Village, near Kiunga. October 1997. Symptoms of fever, diarrhoea, headache, neck pain and stiffness. Died 2 months after admission

Case 3: 18-year-old male from Tabubil (acquired in Kiunga?). February 1998. Symptoms of fever, headache, weakness, vomiting, nausea, body aches, anorexia, constipation. Complete recovery.

Comparison of JE genotypes in the prM gene

Genotype I
- MVE
- TSpig00 (Australia, 2000)
- TS4152 (Australia, 2000)
- Th2372 (Thailand, 1972)
- ThCMAr4384 (Thailand)
- ThCMAr6793 (Thailand, 1993)
- MAPAV294 (Malaysia, 1994)
- K94P05 (Korea, 1994)
- WTP-70-22 (Malaysia, 1970)
- B1065 (Thailand, 1983)
- MaKAr1587 (Malaysia, 1993)
- JKT2363 (Indonesia, 1979)
- JKT2219 (Indonesia, 1979)
- PNG8728 (Papua New Guinea, 1998)
- TS3306 (Australia, 1998)
- FU (Australia, 1995)
- M40 (Australia, 1995)
- PNG1997 (Papua New Guinea, 1997)
- GP78 (India, 1978)
- P20778 (India, 1958)
- Beijing-1 (China, 1949)
- P3 (China, 1949)
- SA14 (China, 1954)
- CH2195 (Taiwan, 1994)
- Indonesia (Indonesia)
- MaKAr60092 (Malaysia, 1992)
- JKT7003 (Indonesia, 1981)
- JKT1749 (Indonesia, 1979)
- JKT9092 (Indonesia, 1981)

Genotype II
- Th2372 (Thailand, 1972)
- ThCMAr6793 (Thailand, 1993)
- MAPAV294 (Malaysia, 1994)
- K94P05 (Korea, 1994)
- WTP-70-22 (Malaysia, 1970)
- B1065 (Thailand, 1983)
- MaKAr1587 (Malaysia, 1993)
- JKT2363 (Indonesia, 1979)
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- MaKAr60092 (Malaysia, 1992)
- JKT7003 (Indonesia, 1981)
- JKT1749 (Indonesia, 1979)
- JKT9092 (Indonesia, 1981)

Genotype III
- JKT9092 (Indonesia, 1981)
- JKT7003 (Indonesia, 1981)
- JKT1749 (Indonesia, 1979)
- JKT9092 (Indonesia, 1981)

Genotype IV
- JKT7003 (Indonesia, 1981)
- JKT1749 (Indonesia, 1979)
- JKT9092 (Indonesia, 1981)

10% divergence
Answers were still needed to two questions:
- Where did the virus come from to spread through PNG? and
- How did it spread from PNG into the Torres Strait of northern Australia
Cyclone Sid
26 December 1997
After the 1998 incursion of JEV into Northern Australia, and especially because of the risk to humans living in Badu, agreement was obtained to build a new communal pig sty some 3km from the township, and to remove all pigs from backyards in the township to the new sty. This had a major effect on the amount of virus in the mosquito population.
Host feeding patterns of *Cx. annulirostris* on Badu Is 2000

- **Horse**: 35.71%
- **Dog**: 2.38%
- **Human**: 61.90%
- **Pig**: 100%

Within community: 61.90%
Outside community: 100%
JEV in Northern Australia – 2

Incursion of topotype 1 JEV

2000: JEV returns to the Torres Strait, with virus isolated from *Culex gelidus*, a major vector of JEV in SE Asia but not previously known to occur in Australia. The JEV strain was different to previous isolates and found to belong to topotype 1, closest to a Korean isolate.


2004: JEV in the Torres Strait and mainland Australia – pig seroconversions and virus isolation from *Cx. sitiens* subgroup mosquito.


2007-2011: No evidence of JEV activity, but limited surveillance has been undertaken. One pig flock near Bamaga by either sentinel pigs nor mosquito trapping for virus isolation – so we really have no idea whether JEV continues to be active or is becoming established.
Comparison of JE genotypes in the prM gene

10% divergence

Genotype I

MVE

Genotype II

TSpig00 (Australia, 2000)
TS4152 (Australia, 2000)

Genotype III

Th2372 (Thailand, 1972)
ThCMAr6793 (Thailand, 1993)
MAPAV294 (Malaysia, 1994)
K94P05 (Korea, 1994)
WTP-70-22 (Malaysia, 1970)
B1065 (Thailand, 1983)
MaKAr1587 (Malaysia, 1993)
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SA14 (China, 1954)
CH2195 (Taiwan, 1994)
Indonesia (Indonesia)
MaKAr60092 (Malaysia, 1992)
JKT7003 (Indonesia, 1981)
JKT1749 (Indonesia, 1979)
JKT9092 (Indonesia, 1981)

Genotype IV

Beijing-1 (China, 1949)
P3 (China, 1949)
SA14 (China, 1954)
CH2195 (Taiwan, 1994)
Indonesia (Indonesia)
MaKAr60092 (Malaysia, 1992)
JKT7003 (Indonesia, 1981)
JKT1749 (Indonesia, 1979)
JKT9092 (Indonesia, 1981)
JEV and its potential to spread

• What will happen next........
• Will it establish in Australia, or Solomon Islands, or further afield??
• Australia and Oceania have the vertebrate hosts and mosquito vectors able to sustain endemic transmission.
• Indeed there are over 3 million feral pigs in Cape York alone.
• However early studies on host preference for feeding by relevant mosquito vectors suggest they might prefer wallabies or possums to pigs, but wallabies and possums may not support JEV replication so well.
• But the same environmental and ecological aspects also occur in PNG where the virus is now widespread.
• Other continents may also have competent vectors and vertebrate hosts, including the North America and Africa.....
Distribution of feral pigs in Australia
Geographic distribution of Cx. *annulirostris* lineages

Hemmerter et al (2007) BMC Evolutionary Biology 7:100
The first cautionary comment!

• Limited or no surveillance is being undertaken in both the Torres Strait and northern mainland Australia.
• Thus we do not really know the situation with respect to JEV activity, or if the virus still exists in Australia.
• However, the virus is endemic now in PNG, and presumably spills over regularly into the Torres Strait and perhaps northern Australia, and
• If Australia is like other places where JEV has emerged and established – why should we be different?
And a second cautionary comment!

- We have shown that immunisation of mice with live attenuated JE vaccine protected mice to subsequent challenge with both virulent JEV and MVEV.
- BUT, while immunisation of mice with inactivated JEV protects in a subsequent challenge with JEV, it can lead to enhancement of the lethality if challenged with MVEV.
- The reverse experiments have also been done with similar results.
- The caution therefore is that inactivated JE vaccine may not be ideal for large scale vaccine usage in Australia.
Vaccines for JEV

• The old vaccine, replaced 3 years ago and no longer available, was an inactivated vaccine made in suckling mouse brains.
• The current vaccine is an inactivated vaccine made in tissue culture.
• The live attenuated SA-14-14-2 vaccine used extensively in China, and more recently in India and Nepal, is not licensed for use in developed countries because of concerns of the biosafety of the cell substrate.
• The next generation of vaccines will be the chimeric JE-YF attenuated virus vaccine – it is already licensed for use in Australia, but will not be available until late in 2012.
• However it might potentially protect against Murray Valley encephalitis and even West Nile, so it remains an interesting enigma!
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