

Japanese encephalitis vaccine: is it being sufficiently used in travellers?

Clinical record

A 32-year-old woman presented to the Royal Brisbane Hospital immediately on disembarking from a flight from Bangkok. She had a 5-day history of gastrointestinal symptoms, fever and altered mental state. She was a university graduate and had travelled for 2 months across south-east Asia before becoming unwell in Phnom Penh, Cambodia. Her illness began with mood elevation, hallucinations, muscle spasms and paraesthesiae, shortly after ingestion of a "herbal pizza". Within 24 hours, nausea, vomiting and profuse watery diarrhoea ensued. Despite empirical treatment for bacterial gastroenteritis, symptoms progressed to lethargy with altered mental state.

The patient had been taking doxycycline for malaria prophylaxis, and had been vaccinated against viral hepatitis, tetanus, poliomyelitis and typhoid. She was aware of the availability of a Japanese encephalitis vaccine, but had been advised that it was not essential.

On presentation, the patient was drowsy and dehydrated, with a temperature of 38°C and tachycardia. There was peripheral leukocytosis (white cell count, 17.9×10^9 cells/L; reference range [RR], $4.0\text{--}11.0 \times 10^9$ cells/L) with dominant neutrophilia, as well as hyponatraemia, but renal function was preserved. Fever and lethargy persisted over 48 hours despite rehydration and regular paracetamol. Increasing obtundation and a fine tremor were observed. The patient complained of persistent headache, mild photophobia and neck discomfort. Her partner commented on her slow mentation, reduced concentration and personality change.

Investigations for malaria, typhoid, rickettsial disease and infectious diarrhoea were all negative. Magnetic resonance imaging of the brain detected no abnormalities. Cerebrospinal fluid (CSF) showed mononuclear pleocytosis (white cell count, 12×10^6 cells/L; 92% mononuclear cells [RR, $< 5 \times 10^6$ mononuclears/L]), with mild elevation of protein level (0.62 g/L [RR, < 0.45 g/L]), but was negative for herpes simplex virus by polymerase chain reaction. Flavivirus-specific IgM was detected in CSF and subsequently blood. The diagnosis of Japanese encephalitis was confirmed by a rise in titre of specific IgG in blood, from 80 (8 days after onset of illness) to 1280 (4 weeks after onset).

The fever resolved spontaneously by Day 4 after presentation, and the patient was discharged after 10 days. At the time of discharge, her level of alertness had improved, but global impairment of higher cognitive functioning and tremor persisted. After a period of convalescence of approximately 5 months, during which she was cared for by her partner, the patient was able to return to work.

and gastrointestinal symptoms.⁴ Japanese encephalitis should therefore be considered among unwell travellers returning from endemic areas, including those with undifferentiated fever.⁴ Blood and CSF are positive for flavivirus antibodies by 10 days after symptom onset. Specific IgM antibody may appear earlier in the CSF. Treatment is symptomatic.

A vaccine is available for Japanese encephalitis and is administered as three doses over 30 days, at a material cost of over \$300. Vaccination is recommended for:

- Travellers spending at least one month in rural areas of Asia or the Western Province of Papua New Guinea, particularly during the wet season, or if there is considerable outdoor activity, or suboptimal accommodation. It is possible that this recommendation will be expanded to include all areas of Papua New Guinea.^{5,6}
- Travellers spending a year or longer in Asia (except Singapore), even if lifestyle is predominantly urban.⁷
- All permanent residents of the outer Torres Strait Islands over the age of 1 year and all non-residents who will be living in the region for 30 or more days during the wet season (December–May).

Vaccine uptake among travellers in whom it should be considered has been hindered by the cost of the vaccine, and by occasional reports of delayed and (rarely) life-threatening adverse reactions.⁸ Overall, local injection-site reactions occur in about 20% of recipients. Systemic reactions, such as fever, rash, myalgia and gastrointestinal symptoms, are seen in about half that number.⁹ A new live, attenuated vaccine that allows a simpler administration regimen and is likely to produce fewer of these adverse reactions than the current vaccine is undergoing Phase II testing.¹⁰ Statistics on vaccine use include military personnel and residents of northern Cape York and the Torres Strait Islands, who receive free vaccinations under the Queensland Government Vaccination Programme. Separate statistics on vaccine use by travellers are unavailable.

Adventure travel is popular among Australians. Uncertainty about disease risks and the financial burden of vaccination and antimalarial prophylaxis combine to make pre-travel counselling a challenge. This case of a rare vaccine-preventable infection with a potentially devastating outcome exemplifies these issues. As an efficacious vaccine for Japanese encephalitis is available, it should be considered for all at-risk travellers. This case also highlights the need to emphasise mosquito avoidance in pre-travel counselling,

Lessons from practice

- Japanese encephalitis is a potentially devastating illness; it can be fatal and can have permanent neurological effects in survivors.
- Vaccination is indicated for many Australians who seek pre-travel counselling; they should be counselled about their risk of contracting Japanese encephalitis and the benefits of the vaccine.
- Mosquito avoidance is a key message in pre-travel counselling.
- Japanese encephalitis may present as an undifferentiated fever; gastrointestinal symptoms may be prominent.

Japanese encephalitis is the leading cause of viral encephalitis in Asia, with recent epidemics in India, Malaysia and Nepal.¹ An outbreak of Japanese encephalitis in the Torres Strait Islands and the northern extremity of Cape York in March 1995² raised concern that this arbovirus may become established in feral pigs in northern Australia. Although the overwhelming majority of infections are asymptomatic, the case-fatality rate of symptomatic infection is 25%–30%, with neuropsychiatric sequelae seen in 30%–50% of survivors.³ The incubation period ranges from 4 to 21 days. The earliest symptoms are lethargy, high fever, headache

SEE ALSO LETTERS, PAGES 282 AND 283

and to consider a broad differential diagnosis in unwell returning travellers.

Catherine M Geraghty,* James S McCarthy†

* Advanced Trainee in General Medicine, Royal Brisbane Hospital Brisbane, QLD; † Associate Professor of Tropical Medicine and Infectious Diseases, Queensland Institute of Medical Research Herston Road, Herston, QLD 4029. j.mccarthy@sph.uq.edu.au

- 1 World Health Organization. Communicable disease surveillance and response. Disease outbreaks. Japanese encephalitis. Available from: www.who.int/disease-outbreak-news/disease/A83.0htm (accessed May 2004).
- 2 Hanna JN, Ritchie SA, Phillips DA, et al. An outbreak of Japanese encephalitis in the Torres Strait, Australia, 1995. *Med J Aust* 1996; 165: 256-260.
- 3 McCormack JG, Allworth AM. Emerging viral infections in Australia. *Med J Aust* 2002; 177: 45-49.
- 4 Watt G, Jongsakul K. Acute undifferentiated fever caused by infection with Japanese encephalitis virus. *Am J Trop Med Hyg* 2003; 68: 704-706.

- 5 Rubin G, Baird J. New recommendation on Japanese encephalitis vaccination for travellers to Papua New Guinea [letter]. *Med J Aust* 2004; 181: 283.
- 6 Hanson JP, Taylor CT, Richards AR, et al. Japanese encephalitis acquired near Port Moresby: implications for residents and travellers to Papua New Guinea [letter]. *Med J Aust* 2004; 181: 282.
- 7 National Health and Medical Research Council. The Australian immunisation handbook. 8th ed. Canberra: NHMRC, 2003.
- 8 Ruff TA, Eisen D, Fuller A. Adverse reactions to Japanese encephalitis vaccine. *Lancet* 1991; 338: 881-882.
- 9 Aventis Pasteur. JE-VAX product information. Sydney: Aventis Pasteur, 1998.
- 10 Monath TP, Guirakhoo F, Nichols R, et al. Chimeric live, attenuated vaccine against Japanese encephalitis (ChimeriVax-JE): phase 2 clinical trials for safety and immunogenicity, effect of vaccine dose and schedule, and memory response to challenge with inactivated Japanese encephalitis antigen. *J Infect Dis* 2003; 88: 1213-1230.

(Received 18 May 2004, accepted 20 May 2004)

□