

POSITION PAPER ON JAPANESE ENCEPHALITIS VACCINES Pediatric Infectious Disease Society of the Philippines *a specialty society of the* Philippine Pediatric Society



BACKGROUND

Japanese encephalitis (JE), a mosquito vector-borne disease, is the leading cause of viral encephalitis and leading cause of childhood neurologic infection and disability in Asia.^{1, 2} It is caused by the JE virus and is transmitted by the mosquito *Culex tritaeniorhynchus*, which breeds in water pools and flooded rice fields. JE is a zoonotic disease that exists in animals but can infect humans; the JE virus multiplies to reach high levels in pigs and aquatic birds, which serve as amplifying hosts. A mosquito vector which has taken a blood meal from an infected animal host can bite humans, who then may develop infection or actual disease.

Most JE virus infections are either asymptomatic or mild (fever and headache), but 1 in 250 infections results in severe illness. This can present as rapid onset of high fever, headache, neck stiffness, disorientation, coma, seizures, paralysis and ultimately death. The fatality rate can be as high as 30% among those with disease symptoms; some 30-50% of survivors suffer from neurologic sequelae.² Young children <10 years are more likely to die or have residual neurologic deficits.² There is currently no treatment for JE.

EPIDEMIOLOGY

Based on the World Health Organization (WHO) estimates, 68,000 cases of JE occur annually, with 3 billion people living in 24 South-East Asian and Western Pacific regions at risk for transmission of the virus, including the Philippines.⁴

The Japanese encephalitis virus (JEV) was first reported in the Philippines in 1943 and since then, the Philippines has been recognized as a country where the virus normally circulates. ¹ A local epidemiologic study using seroepidemiologic and clinical JE studies, animal and mosquito surveys, and national surveillance data, confirmed that the JE virus is found year-round in all regions of the country.⁵

The JE virus was found to be the causative agent in 7 – 18% of clinical meningitis and encephalitis cases, and 16 – 40% of clinical encephalitis cases. Majority of JE cases occurred in children below 15 years of age, while individuals older than 18 years comprised 15% of cases.⁵ In 2016, there were a total of 313 laboratory-confirmed JE cases reported, which was 152% higher than 2015, when 124 cases were reported.⁶

Based on the data available from the Department of Health Acute Meningitis Encephalitis Syndrome (AMES) Surveillance Report from 01 January to 01 July 2017, the number of cases reported was 27% lower compared to the same period in 2016.⁷ According to the data communicated by the DOH in their recent press release, as of 26 August 2017, the DOH Epidemiology Bureau has recorded a 44% decrease of laboratory confirmed JE cases all over the country as compared to the same period last year.⁸

The Philippines is thus included in the list of countries where JE virus is usually found. The peak season for transmission is not yet well defined, and based on the most recent data, the number of cases being reported is decreasing.

DISEASE PREVENTION

JE is considered a significant public health threat. The World Health Organization recommends the following main activities to address this concern: strengthening JE surveillance, ensuring adequate resources for JE vaccination, and sustaining national commitment to JE prevention and control.¹

The true extent of the virus and burden of disease is not well understood in areas where JE surveillance is not well established. Thus, the WHO recommends a strengthened surveillance system for every at-risk country, to assess the burden of disease and monitor safety, impact, and effectiveness of JE vaccines. At present, 22 out of 24 countries with JE virus transmission risk have conducted JE surveillance, including the Philippines. JE has been part of the list of notifiable diseases under the Philippine Integrated Disease Surveillance and Response (PIDSR) surveillance since 2009.

Since JE is a zoonotic disease, it can never be eradicated. However, there is little evidence to support effectiveness in disease reduction by approaches such as vaccination of pigs, or environmental (e.g. mosquito nets) and chemical control of vectors. These methods cannot be relied on to reduce disease incidence, and should not divert efforts from childhood JE vaccination programs.

The best evidence to support a reduction in JE disease burden points to vaccination of humans.^{2,3} Disease control relies on individual protection because there is no herd immunity with JE.² Elimination of clinical disease is possible through vaccination of populations at risk. In fact, the integration of JE vaccine into the immunization programs of Japan, South Korea, Taiwan and Thailand has led to the near elimination of disease in these countries.

The impact of vaccination programs as an intervention during outbreaks of JE has not been studied. If an outbreak occurs in an area where JE vaccination has not yet been introduced, it is important to assess whether an immediate vaccine response will be useful, taking into consideration the following: (1) size of the outbreak, (2) timeliness of the response, (3) population affected, and (4) programmatic capacity. If vaccination is to be included as an outbreak response, this should be followed by a plan for introduction into the routine immunization schedule.³

CURRENT VACCINE RECOMMENDATIONS

1. World Health Organization Recommendations:

The WHO recommends that JE vaccination should be included in the national immunization program of a country where JE has been found to be a public health threat. In addition, the WHO recommends JE vaccination for travelers with extensive outdoor exposure during the transmission season.

2. PIDSP/PPS/PFV 2017 Recommendations:

Currently, the only available Philippine FDA registered JE vaccine in the country is the live attenuated recombinant (chimeric) vaccine. The minimum age of administration is 9 months, to be given subcutaneously. For children 9 months to 17 years of age, a booster dose should be given 12-24 months after the primary dose. For individuals 18 years and older, a single dose is recommended.

SUMMARY STATEMENT

The Philippine Pediatric Society (PPS) and the Pediatric Infectious Disease Society of the Philippines (PIDSP) recognize that Japanese encephalitis is an important public health problem in the Philippines. Although relatively few cases are reported, the severity of the disease, its high case-fatality rates and the complications of JE present a significant burden to the community. JE vaccination has been incorporated in the recommendations for childhood immunization by the PPS/PIDSP/PFV since 2016. In

the recent months there have been increased demand for the vaccine due to alleged increase in the number of JE cases.

The unfortunate situation of misinformation, especially through social media, has forced health care providers to seek guidance regarding the best possible use of scarce vaccine supply. Thus, the PPS and PIDSP, through this position paper, propose these recommendations:

- 1. JE is a reportable disease and surveillance must be sustained; healthcare providers from public and private sectors must actively participate in the government's efforts to accurately monitor JE disease in the Philippines.
- 2. Health care providers and public health authorities must remain the most reliable sources of information; they are enjoined to actively communicate relevant evidence-based data and interpret these for the public to avoid undue panic and to advise on the most appropriate measures to take. Any effort by the lay public in communicating about JE disease and prevention should ensure that the references used are reputable and based on real scientific medicine.
- 3. Prevention methods such as mosquito vector control, personal protective measures (mosquito repellents, bed nets), and others, may be used but must not deter individuals from seeking JE vaccination, which is the only method proven highly effective for prevention.
- 4. JE Vaccination continues to be recommended for children ≥9 months of age as part of their immunization schedule. In times of scarce supply, priority should be given to those most at risk, i.e. children <15 years of age and those living in high risk areas. The use of currently available JE vaccines should follow the manufacturer's recommendations.</p>

References:

- 1) Word Health Organization. Japanese Encephalitis: surveillance and immunization in Asia and the Western Pacific, 2016. MMWR June 2017; 23 (92): 321-332.
- Halstead S et al. Japanese Encephalitis Vaccines. In Plotkin S, Orenstein W, Offit P, editors. Vaccines 7th: Elsevier; 2018, pp 511-548.
- World Health Organization. Japanese encephalitis Vaccines: WHO position paper Feb 2015. WER Feb 2015; 9 (90): 69-88.
- 4) Campbell G et al. Estimated global incidence of Japanese encephalitis: a systematic review. Bull World Health Organ 2011; 89: 766-774E.
- 5) Lopez A et al. Epidemiology of Japanese Encephalitis in the Philippines: A Systematic Review. PLOS Neglected Trop Dis, March 20,2015.
- 6) Department of Health Epidemiology Bureau. Weekly Disease Surveillance Report MW 52: Jan 1 to Dec 31, 2016.
- 7) Department of Health Epidemiology Bureau. Acute Meningitis Encephalitis Syndrome Surveillance Report MW 26: January 1 July 1 2017.
- 8) DOH Press Release September 06 2017.
- 9) Batchelor P and Petersen K. Japanese encephalitis: a review of clinical guidelines and vaccine availability in Asia. Trop Dis, Travel Med and Vaccines (2015) 1:11.
- 10) Nagendra R. Hegde & Milind M. Gore (2017): Japanese encephalitis vaccines: Immunogenicity, protective efficacy, effectiveness, and impact on the burden of disease. Human Vaccines & Immunotherapeutics, Feb 2017. DOI: 10.1080/21645515.2017.1285472