Japanese Encephalitis : Is Routine Immunization Required?

Brig Zile Singh*, Lt Col VK Agarwal[†]

Abstract

Japanese encephalitis is the leading cause of viral encephalitis in Asia. In endemic areas annual incidence ranges from 10-100 per 100000 population. Case fatality averages 30% and a high percentage of the survivors are left with permanent neuropsychiatric sequelae. There is no effective drug treatment for this disease. In recent decades, Japanese encephalitis virus has caused epidemics in previously unaffected countries like India, Myanmar, Nepal, Sri Lanka, Thailand and Viet Nam. No effective environmental control is known. Although socioeconomic improvement and changes in agricultural practices are likely to reduce viral transmission, large-scale vaccination of affected populations with an effective and affordable vaccine appears logical at least in the short term. The impact of large-scale Japanese Encephalitis vaccination is documented in some regions of China and systematic vaccination has contributed to significant decline in incidence in Japan, Republic of Korea and Thailand.

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Introduction

Japanese encephalitis (JE) is an important form of viral encephalitis causing at least 50000 cases and 10000 deaths each year, mostly among children [1]. In recent years, Japanese encephalitis has spread to newer geographic locations like Australia and Pakistan [2].

JE is a disease of public health importance because of its epidemic potential and high fatality rate. In patients who survive, complications lead to life long sequelae. The first major out break of JE occurred in Bankura and Burdwan districts of West Bengal in 1973 and since then it has spread to many states and UTs of the country [3]. High incidence of JE was reported in Andhra Pradesh, Orissa, West Bengal and UP in 2003. Pattern of JE transmission varies between countries and from year to year. In endemic areas, the annual incidence of disease ranges from 10-100 per 100000 population [4]. The vast majority (85 percent) occur among children less than 15 years of age. Nearly 10 percent are among those over 60 years perhaps reflecting waning protective immunity.

Currently, there is a joint initiative by the South-East Asia, Eastern Mediterranean, Western Pacific and European Regional Offices of WHO, UNICEF Regional Office for South Asia and the Bill and Melinda Gates Children's Vaccine Program (CVP) to promote introduction of JE vaccine for routine immunization in

countries where the disease is a public health concern.

Problem in India

Reconjugation of JE, based on serological surveys, was first made in 1955 in Tamil Nadu. Subsequent surveys carried out by National Institute of Virology, Pune indicated that about half the population in South India has neutralizing antibodies to the virus. In the last decade, there has been a major upsurge of JE in Assam, Andhra Pradesh, Bihar, Goa, Karnataka, Manipur, Maharashtra, Madhya Pradesh, Tamil Nadu, UP, Pondichery and West Bengal. JE incidence during the past few years is given in Table 1.

Table 1
Incidence of Japanese Encephalitis in India

Years	Cases	Deaths
1996	2246	593
1997	2516	632
1998	2090	507
1999	3428	680
2000	2593	556
2001	1171	303
2002	3251	641

Children are mainly affected, with morbidity rate estimated at 0.3 to 1.5 per 100000 populations. Fatality rate ranged from 10% to 60% and 50% of those who recover left are with neurological deficit. Incidence is

*ADH & Sr Adv (PSM), Military Hospital, Jalandhar, [†]Reader, Department of PSM, Armed Forces Medical College, Pune-40.

higher in males but subclinical infection has occurred equally in both sexes [5].

Causative agent

JE is caused by a group B arbovirus (flavivirus). The virus is antigenically related to other flaviviruses like dengue, yellow fever and west Nile virus.

Mode of transmission

The infection is transmitted through the bite of an infected Culicine mosquito. In human beings, viraemia is mild and lasts for a short duration. Infection in man is the dead end of transmission. Man to man transmission has not been documented [1].

Reservoir of infection

The animal hosts include pigs, cattle and horses. Water birds such as pond herons, cattle egrets, poultry birds and ducks play a significant role in the natural history of JE virus. Infected pigs do not manifest overt symptoms but they develop tremendous viraemia. The pigs are considered amplifying hosts. Currently available evidence does not indicate major role for cattle in transmission of JE.

Vectors

Culicine mosquitoes, notably *Culex tritaeniorhynchus*, *Culex vishnui* and *Culex gelidus* along with some anophelines have been incriminated as vectors of JE. Among these, *Culex tritaeniorhynchus* is implicated as the most important vector in south India [6] and in several other JE affected areas in India [7,8]. These mosquitoes breed in irrigated rice fields, shallow ditches and pools. These mosquitoes are zoophilic and feed primarily on vertebrate hosts.

Clinical manifestation

The incubation period in man following a mosquito bite varies from 4-14 days. Not all individuals bitten develop disease. The ratio of overt disease to inapparent infection varies from 1:300 to 1:1000. Encephalitis due to JE shows a scattered distribution. The course of disease in man may be divided into prodromal, acute, late stage and sequelae phase. The fatality varies between 20-40 percent, but may reach over 58 percent. The average period between the onset of illness and death is 9 days.

Aetiological diagnosis of JE is based on serological testing using ELISA that detects specific IgM in the CSF or in blood of almost all patients within 4-7 days of onset of disease. Other diagnostic methods include dot-blot or immunoprecipitation IgM assay suitable for field use and to monitor changes of JE specific antibody titers in sequential serum samples [1].

Prevention and control

A surveillance system should be established so that any case of encephalitis is immediately reported to the local health authority. Necessary field investigation must be carried out to check for amplifying host and vector. The preventing measures are directed at reducing vector density by insecticides and personal protection to prevent bite of mosquitoes. The isolation and destruction of the amplifying hosts is not practiced as those animals do not show any overt signs of illness.

JE vaccination is the single most important control measure. Currently three types of JE vaccines are in large-scale use. A mouse brain-derived and inactivated vaccine based on the Nakayama strain or on Beijing –1 strain (seroconversion rate 80% to 90%) is produced in several Asian countries and is available in the international market. A cell culture derived inactivated vaccine (seroconversion rate 85%) and a cell culture live attenuated vaccine (seroconversion rate 94% to 100%) are produced in China and used within the Chinese JE control program. Controlled studies performed in 2 different endemic regions have shown that mouse brain derived vaccine is efficacious and without serious side-effects for children. In a prospective study among United States military personnel in Japan, the overall allergic reaction was 0.6% [1]. National immunization program with inactivated mouse brain derived vaccine has reduced illness and death due to JE in South Korea but adverse effects of vaccine are increasing and a national compensation program for vaccine injury was begun in 1995 [9]. In the large scale vaccination against JE, impact is documented in Sri Lanka and Thailand. Systemic vaccination was even more successful and resulted in virtual elimination of the disease in Japan, Taiwan, South Korea and most parts of China [10].

A killed JE vaccine was produced at the Central Research Institute (CRI), Kasauli from the brain of suckling mice inoculated with Nakayama JE strain. The vaccine is not recommended for use for the control of an outbreak. Two doses of 1ml IM each (0.5ml for children under age of 3 years) should be administered at an interval of 7-14 days. A booster of 1 ml should be given after a few months (before 1 year) in order to develop full protection. Revaccination may be given after 3 years. Since the risk of JE is not universal and is limited to focal areas, JE vaccination is not included in the national immunization programme in India [3]. But inclusion of an effective and affordable vaccine for JE in endemic areas in India will reduce mortality and life long sequelae and prevent further spread.

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Quiz

Clinicopathological Quiz

Lt Col S Gokhale, Retd^{*}, Col AK Malaviya⁺, Lt Col A Basu[#], Lt Col SJ Varghese (Retd)^{**}, Maj A Agarwal⁺⁺

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A 48-year old serving JCO reported on 15 May 2002 with two months history of dull, persistent and localized pain in the lower abdomen and recurrent hiccups and vomiting of ten days duration. His pulse was 84/min and blood pressure was 94/60mmHg. There was slight unsteadiness of gait with depressed deep tendon jerks, cerebellar signs with impaired tandem walking and slurred speech. Haemogram, biochemical parameters and USG abdomen were normal. UGI endoscopy revealed pangastritis. MRI showed lacunar infarcts in left middle and posterior cerebral artery territories. He was treated for pangastritis with clarithromycin, amoxycillin and omeprazole. Brain stem stroke was suspected and he was put on chlorpromazine and perinorm.

He developed fever (103.8° F) and abnormal behavior on 17 Jun 02, had peripheral cyanosis, 110/min pulse,

60mm Hg systolic blood pressure and unrecordable diastolic pressure. ECG revealed tall t waves in leads II, III, avF, V1 - V4. Possibilities of cerebral malaria and heat stroke were considered and patient was put on injection quinine, dopamine, dobutamine, cefotaxime, amikacin, hydrocortisone and oxygen inhalation.

Patient recovered by 19th June. On 30th of June patient developed 101.2°F fever, abnormal behaviour, 106/min pulse and 80/60 mm Hg BP. He was given injection quinine, positive inotropic agents and broad-spectrum antibiotics. Patient died on 1 July 2002. Investigations including urine, blood counts, LFT, renal function tests, S electrolytes, cholesterol, PT and PTTK were normal. Autopsy was performed to ascertain the diagnosis.

What is your diagnosis?

Answer to the quiz - page 397

^{*}Former Classified Specialist (Pathology & Microbiology), ⁺Sr Adv (Pathology), Command Hospital (CC) Lucknow 226002, [#]Classified Specialist (Pathology), Command Hospital (SC), Pune 411040, ^{**}Former Associate Professor, Dept of Pathology, AFMC, Pune 411040, ⁺⁺Graded Specialist (Pathology), 167 MH, C/O 56 APO.

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