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RESEARCH ARTICLE

BRAIN FEVER THAT WREAK HAVOC IN NORTHERN DISTRICTS OF WEST BENGAL – A DEVASTATING TALE OF KILLING POWER OF JAPANESE ENCEPHALITIS

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ABSTRACT

In Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia, with up to 70,000 cases reported annually. Case-fatality rates range from 0.3% to 60% and depend on the population and age. Rare outbreaks in U.S. territories in the Western Pacific have also occurred. Residents of rural areas in endemic locations are at highest risk; Japanese encephalitis does not usually occur in urban areas. The districts situated in northern Bengal witnessed massive loss of life to a deadly fever coupled with tremor, rigidity & convulsion in later half of 2014 which results loss of more than 100 lives in northern West Bengal. Japanese encephalitis is a serious threat to particularly rural population and those lived closely to forest and involved in animal husbandry ,and the main multiplier pigs do not show any symptom of infestation apart from pregnant sows that faces abortion threat, though 1 in 250 develop deadly encephalitis but recent outbreak clearly delineates its devastating effect on human life. World health organization stresses on the need for increased regional and national awareness of JE and for international support to control the disease is urgent. JE vaccination should be extended to all areas where JE is a demonstrated public health problem. The most effective immunization strategy in JE endemic settings is a onetime campaign in the primary target population, as defined by local epidemiological data, followed by incorporation of the JE vaccine into the routine immunization programme. This approach has a greater public health impact than either strategy separately.

INTRODUCTION

The districts situated in northern Bengal witnessed massive loss of life to a deadly fever coupled with tremor, rigidity & convulsion in later half of 2014 which results loss of more than 100 lives in northern West Bengal. Causative agent Japanese encephalitis virus is an enveloped virus of the genus flavivirus and is closely related to the West Nile virus and St. Louis encephalitis virus. The positive sense single stranded RNA genome is packaged in the capsid which is formed by the capsid protein. The outer envelope is formed by envelope protein and is the protective antigen. It aids in entry of the virus to the inside of the cell (He, 2006 and Su *et al*., 2002). The virus appears to have originated from its ancestral virus in the mid-1500s in the Indonesia-Malaysia region and evolved there into five different genotypes and spread across Asia (Mohammed *et al*., 2011). Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asia, with up to 70,000 cases reported annually (Campbell *et al*., 2011).

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Case-fatality rates range from 0.3% to 60% and depend on the population and age. Rare outbreaks in U.S. territories in the Western Pacific have also occurred. Residents of rural areas in endemic locations are at highest risk; Japanese encephalitis does not usually occur in urban areas. Countries which have had major epidemics in the past, but which have controlled the disease primarily by vaccination, include China, [Republic of Korea], Japan, Taiwan and Thailand. Other countries that still have periodic epidemics include Vietnam, Cambodia, Myanmar, India, Nepal, and Malaysia. Japanese encephalitis has been reported on the Torres Strait Islands and two fatal cases were reported in mainland northern Australia in 1998. There were reported cases in Kachin State, Myanmar in 2013. The spread of the virus in Australia is of particular concern to Australian health officials due to the unplanned introduction of Culex gelidus, a potential vector of the virus, from Asia. However, the current presence on mainland Australia is minimal. Human, cattle and horses are dead-end hosts as the disease manifests as fatal encephalitis. Swine acts as an amplifying host and has a very important role in the epidemiology of the disease. Infection in swine is asymptomatic, except in pregnant sows, when abortion and fetal abnormalities are common sequelae. The most important vector is Culex tritaeniorhynchus, which feeds on cattle in

preference to humans. It has been proposed that moving swine away from human habitation can divert the mosquito away from humans and swine. The natural hosts of the Japanese encephalitis virus are birds, not humans, and many believe the virus will therefore never be completely eliminated (Ghosh and Basu, 2009). In November 2011, the Japanese encephalitis virus was reported in Culex bitaeniorhynchus in the Republic of Korea (Kim, Heung Chul *et al*., 2011). Though most cases are asymptomatic and 1 in 250 develop deadly encephalitis, this mosquito-borne arboviral disease and is the leading cause of morbidity and mortality in South East Asia. The outcome of JE can be fatal in 25 per cent of cases, and it may also result in residual sequelae in 30 to 60 per cent of cases (Gajanana, 1998 and Kanojia *et al*., 2003). In India, the disease was first reported in 1955 and subsequently many epidemics have occurred in different parts of the country (Gajanana, 1998; Kanojia *et al*., 2003; Rao and Arunachalam, 2010; Mourya *et al*., 1989 and Mishra, 1984). JE virus (JEV) infects a large number of susceptible individuals but only a few develop overt manifestations of the disease (George *et al*., 1990) JE is principally a disease of rural agricultural areas, where vector mosquitoes proliferate in close association with pigs, which are the principal vertebrate amplifying hosts.

Large aquatic birds may sub serve this function in areas where pigs are absent. Humans are incidental to the transmission cycle (Chakravarty *et al*., 1975 and Rajagopalan and Panicker, 1978). The seasonal incidence of JE varies in different parts of India. In West Bengal, the disease occurred between May and October, and was shown to be related to the summer monsoon. In Assam and Uttar Pradesh epidemics have occurred between September and December (Reuben and Gajanana, 1997). During 2011-2012, JE outbreaks occurred in many parts of north eastern states including Bihar and North West Bengal. During the recent outbreak JE cases were reported from four different districts (i.e. Cooch Behar, Dakshin Dinajpur, Darjeeling and Jalpaiguri) of North West Bengal from the first quarter of 2011 onwards (Reuben and Gajanana, 1997). A study conducted on paediatric in Burdwan, Bankura, Purulia and Midnapore population in a community occupying lowest level of society and are closely associated with pig shows clearly that this population are vulnerable to JE VIRUS and in case of any outbreak they run the risk of being hardly hit (Chatterjee *et al*.,2004).

Human, cattle and horses are dead-end hosts as the disease manifests as fatal encephalitis. Swine acts as an amplifying host and has a very important role in the epidemiology of the disease. Infection in swine is asymptomatic, except in pregnant sows, when abortion and foetal abnormalities are common sequelae. The most important vector is *Culex tritaeniorhynchus*, which feeds on cattle in preference to humans. It has been proposed that moving swine away from human habitation can divert the mosquito away from humans and swine. The natural hosts of the Japanese encephalitis virus are birds, not humans, and many believe the virus will therefore never be completely eliminated (Ghosh and Basu, 2009). In November 2011, the Japanese encephalitis virus was reported in *Culex bitaeniorhynchus* in the Republic of Korea (Kim Heung Chul *et al*., 2011). There is no specific treatment for Japanese encephalitis and treatment is supportive; (Solomon *et al*., 2000) with assistance given for feeding, breathing or seizure control as required. Raised intracranial pressure may be managed with mannitol (*Japanese encephalitis~treatment* at eMedicine). There is no transmission from person to person and therefore patients do not need to be isolated. A breakthrough in the field of Japanese encephalitis therapeutics is the identification of macrophage receptor involvement in the disease severity. A recent report of an Indian group demonstrates the involvement f monocyte and macrophage receptor CLEC5A in severe inflammatory response in Japanese Encephalitis infection of the brain. This transcriptomicstudy provides a hypothesis of neuroinflammation and a new lead in development of appropriate therapeutic against Japanese encephalitis (Ghosh and Basu, 2009 and Kim Heung Chul *et al*., 2011). Infection with Japanese Encephalitis confers lifelong immunity. There are currently three vaccines available: SA14-14-2, IC51 (marketed in Australia and New Zealand as JESPECT and elsewhere as IXIARO) and Chimeri Vax-JE (marketed as IMOJEV) (Solomon, 2006). All current vaccines are based on the genotype III virus.

A formalin-inactivated mouse-brain derived vaccine was first produced in Japan in the 1930s and was validated for use in Taiwan in the 1960s and in Thailand in the 1980s. The widespread use of vaccine and urbanization has led to control of the disease in Japan, Korea, Taiwan and Singapore. The high cost of this vaccine, which is grown in live mice, means that poorer countries have not been able to afford to give it as part of a routine immunization program (Schiøler *et al*., 2007). The neutralizing antibody persists in the circulation for at least two to three years, and perhaps longer (Gambel *et al*., 1995 and Kurane and Takashi, 2000). The total duration of protection is unknown, but because there is no firm evidence for protection beyond three years, boosters are recommended every three years for people who remain at risk (Solomon, 2006). Furthermore there is also no data available regarding the interchangeability of other JE vaccines and IXIARO and recommended those previously immunised with other JE vaccines receive Green Cross or JE-Vax or a primary course of IXIARO. In September 2012 an Indian firm Biological E Limited has launched an Inactivated Cell culture derived vaccine based on SA 14-14-2 strain which was developed in a Technology transfer agreement with Intercell and is a thiomersal-free vaccine (Our Bureau, Alison Bryant, 2013).

Though till date vaccination seems to be only sure shot preventive and protective measure ,research are on in full swing to found new avenue that can give new ray of hope in combating this menace, number of drugs have been investigated to either reduce viral replication or provide neuroprotection in cell lines or studies upon mice. Though none are currently advocated in treating human patients but animal studies shows encouraging results use of rosmarinic acid, (Swarup *et al*., 2007) arctigenin, (Swarup *et al*., 2008) and oligosaccharides with degree of polymerization 6 from Gracilaria sp. or Monostroma nitidum (Kazłowski *et al*., 2012) have been shown to be effective in a mouse model of Japanese encephalitis. Curcumin has been shown to impart neuroprotection against Japanese Encephalitis infection in an in vitro study. Curcumin possibly acts by decreasing cellular reactive oxygen species level, restoration of cellular membrane integrity, decreasing pro-apoptotic signaling molecules, and modulating cellular levels of stress-related proteins. It has also been shown that the production of infective viral particles

from previously infected neuroblastomacells are reduced, which is achieved by the inhibition of ubiquitin-proteasome system (Dutta *et al*., 2009). Minocycline in mice resulted in marked decreases in the levels of several markers, viral titre, and the level of proinflammatory mediators (Mishra and Basu, 2008) and also prevents barrier damage (Mishra *et al*., 2009). Japanese encephalitis is a serious threat to particularly rural population and those lived closely to forest and involved in animal husbandry, and the main multiplier pigs do not show any symptom of infestation apart from pregnant sows that faces abortion threat, though 1 in 250 develop deadly encephalitis but recent outbreak clearly delineates its devastating effect on human life. World health organization stresses on the need for increased regional and national awareness of JE and for international support to control the disease is urgent. JE vaccination should be extended to all areas where JE is a demonstrated public health problem. The most effective immunization strategy in JE endemic settings is a onetime campaign in the primary target population, as defined by local epidemiological data, followed by incorporation of the JE vaccine into the routine immunization programme. This approach has a greater public health impact than either strategy separately (http://www.who.int/ biologicals/areas/vaccines/jap_encephalitis/en/)

REFERENCES

He, B. March 2006. "Viruses, endoplasmic reticulum stress, and interferon responses". *Cell Death Differ.* 13(3): 393–403. doi:10.1038/sj.cdd.4401833.PMID 16397582.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC155064/ - Su, HL., Liao, CL. and Lin, YL. May 2002. "Japanese encephalitis virus infection initiates endoplasmic reticulum stress and an unfolded protein response". *J. Virol.* 76(9): 4162–71. doi:10.1128/JVI.76.9.4162-4171.2002. *PMC* 155064. PMID 11932381.

Gajanana, A. 1998. Epidemiology and surveillance of Japanese encephalitis in Tamil Nadu. ICMR Bull; 28: 33-7.

Kanojia, PC., Shetty, PS. and Geevarghese, G. 2003. A long-term study on vector abundance & seasonal prevalence in relation to the occurrence of Japanese encephalitis in Gorakhpur district, Uttar Pradesh. *Indian J Med Res*; 117: 104-10.

Gajanana, A. 1998. Epidemiology and surveillance of Japanese encephalitis in Tamil Nadu. ICMR Bull; 28: 33-7.

Kanojia, PC., Shetty, PS. and Geevarghese, G. 2003. A long-term study on vector abundance & seasonal prevalence in relation to the occurrence of Japanese encephalitis in Gorakhpur district, Uttar Pradesh. *Indian J Med Res*; 117: 104-10.

US, Rao, MS. and Arunachalam, N. 2010. The effects of climatic factors on the distribution and abundance of Japanese encephalitis vectors in Kurnool district of Andhra Pradesh, India. *J Vector Borne Dis*; 47: 26-32.

Mourya, DT., Ilkal, MA., Mishra, AC., Jacob, PG., Pant, U., Ramanujam, S. *et al*. 1989. Isolation of Japanese encephalitis virus from mosquitoes collected in Karnataka state, India from 1985 to 1987. *Trans R Soc Trop Med Hyg*; 83: 550-2.

icmr.nic.in/ijmr/2003/0302.pdf - Mishra, AC., Jacob, PG., Ramanujam, S., Bhat, HR. and Pavri, KM. 1983. Mosquito vectors of Japanese encephalitis epidemic in Mandya district (India). *Indian J Med Res* 1984; 80: 377-89.

George, S., Yergolkar, PN., Kamala and Kamala, CS. 1990. Outbreak of encephalitis in Bellary district of Karnataka & adjoining areas of Andhra pradesh. *Indian J Med Res*; 91: 328-30.

Chakravarty, SK., Sarkar, JK., Chakravarty, MS., Mukherjee, MK. and Mukherjee, KK. 1975. The first epidemic of Japanese encephalitis studied in India-virological studied. *Indian J Med Res*; 63: 77-82.

Rajagopalan, PK. and Panicker, KN. 1978. A note on the 1976 epidemic of Japanese encephalitis in Burdwan district, West Bengal. *Indian J Med Res*; 68: 3938

Reuben, R. and Gajanana, A. 1997. Japanese encephalitis in India. *Indian J Pediatr*; 64: 243-51.

Campbell, GL., Hills, SL., Fischer, M., Jacobson, JA., Hoke, CH., Hombach, JM., Marfin, AA., Solomon, T., Tsai, TF., Tsu, VD. and Ginsburg, AS. November 2011. "Estimmated global incidence of Japanese encephalitis: a systematic review". *Bull World Health Organ* 89 (10): 766–74.doi:10.2471/BLT.10.085233. PMID 3209971.

Ghosh, D. and Basu, A. September 2009. "Japanese encephalitis-a pathological and clinical perspective". In Brooker, Simon. *PLoS Negl Trop Dis* 3 (9): e437.doi:10.1371/journal.pntd.0000437. PMC 2745699.P MID 19787040.

Kim Heung Chul, Terry A. Klein, Ratree Takhampunya, Brian P. Evans, Sirima Mingmongkolchai, Ampornpan Kengluecha, John Grieco, Penny Masuoka, Myung-Soon Kim, Sung-Tae Chong, Jong-Koo Lee and Won-Ja Lee. 2011. Japanese Encephalitis Virus in Culicine Mosquitoes (Diptera: Culicidae) Collected at Daeseongdong, a Village in the Demilitarized Zone of the Republic of Korea. *Journal of Medical Entomology* 48(6): 1250-1256.

Mohammed, MA., Galbraith, SE., Radford, AD., Dove, W., Takasaki, T., Kurane, I. and Solomon, T. July 2011. "Molecular phylogenetic and evolutionary analyses of Muar strain of Japanese encephalitis virus reveal it is the missing fifth genotype". *Infect Genet Evol* 11 (5): 855–62.doi:10.1016/j.meegid.2011.01.020. PMID 21352956.

Kim Heung Chul, Terry A. Klein, Ratree Takhampunya, Brian P. Evans, Sirima Mingmongkolchai, Ampornpan Kengluecha, John Grieco, Penny Masuoka, Myung-Soon Kim, Sung-Tae Chong, Jong-Koo Lee and Won-Ja Lee. 2011. Japanese Encephalitis Virus in Culicine Mosquitoes (Diptera: Culicidae) Collected at Daeseongdong, a Village in the Demilitarized Zone of the Republic of Korea. *Journal of Medical Entomology* 48(6): 1250-1256.

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Solomon, T., Dung, NM., Kneen, R., Gainsborough, M., Vaughn, DW. and Khanh, VT. 2000. "Japanese encephalitis". *Journal of Neurology Neurosurgery and Psychiatry* 68 (9): 405–15. doi:10.1136/jnnp. 68.4.405. PMC 1736874.

www.ncbi.nlm.nih.gov/pubmed/20637688 -Nimesh Gupta, Vinay Lomash and P.V. Lakshmana Rao September 2010. "Expression profile of Japanese encephalitis virus induced neuroinflammation and its implication in disease severity". *Journal of Clinical Virology* 49 (1): 04–10. doi:10.1016/j.jcv.2010.06.009. PMID 20637688.

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3058095/ - Nimesh Gupta and P.V. Lakshmana Rao, March 2011. "Transcriptomic profile of host response in Japanese encephalitis virus infection". *Virology Journal* 8(92):

92. doi:10.1186/1743-422X-8-92. PMC 3058095.PMID 21371334.

Schiøler, KL., Samuel, M. and Wai, KL. 2007. "Vaccines for preventing Japanese encephalitis". *Cochrane Database Syst Rev* (3): CD004263.doi:10.1002/14651858. CD004263.pub2. PMID 17636750.

Solomon, T. 2006. "Control of Japanese encephalitis - within our grasp?". *New England Journal of Medicine* 355(9): 869–71. doi:10.1056/NEJMp058263. PMID 16943399.

cid.oxfordjournals.org/content/35/2/183.full - Gambel, JM., DeFraites, R., Hoke, C. *et al.* 1995. "Japanese encephalitis vaccine: persistence of antibody up to 3 years after a three-dose primary series (letter)". *J Infect Dis* 171 (4): 1074. doi:10.1093/infdis/171.4.1074.PMID 7706798.

epo.wikitrans.net/Japanese_encephalitis - Kurane, I. and Takashi, T. 2000. "Immunogenicity and protective efficacy of the current inactivated Japanese encephalitis vaccine against different Japanese encephalitis virus strains". *Vaccine* 18 (Suppl): 33–5. doi:10.1016/ S0264-410X(00)00041-4. PMID 10821971.

Solomon, T. 2006. "Control of Japanese encephalitis - within our grasp?". *New England Journal of Medicine* 355(9): 869–71. doi:10.1056/NEJMp058263.PMID 16943399.

epo.wikitrans.net/Japanese_encephalitis - "Jeev an inactivated Japanese Encephalitis vaccine launched in Hyderabad". Our Bureau, Hyderabad. 15 September 2012. Retrieved 11 January 2013

Alison Bryant, 17 September 2012. "Intercell's Jeev vaccine debuts in India". Retrieved 11 January 2013.

Swarup, V., Ghosh, J., Ghosh, S., Saxena, A. and Basu, A. September 2007. "Antiviral and anti-inflammatory effects of rosmarinic acid in an experimental murine model of Japanese encephalitis". *Antimicrob. Agents Chemother.* 51 (9): 3367–70. doi:10.1128/AAC.00041-07.PMC 2043228. PMID 17576830.

Swarup, V., Ghosh, J., Mishra, MK. and Basu, A. March 2008."Novel strategy for treatment of Japanese encephalitis using arctigenin, a plant lignan". *J. Antimicrob. Chemother.* 61 (3): 679–88. doi:10.1093/jac/dkm503. PMID 18230688.

Kazłowski, B., Chiu, YH., Kazłowska, K., Pan, CL. and Wu, CJ. August 2012. "Prevention of Japanese encephalitis virus infections by low-degree-polymerisation sulfated saccharides from *Gracilaria* sp. and *Monostroma nitidum*". *Food Chem* 133 (3): 866–74.doi:10.1016/j.foodchem. 2012.01.106.

Dutta, K., Ghosh, D. and Basu, A. May 2009. "Curcumin Protects Neuronal Cells from Japanese Encephalitis Virus-Mediated Cell Death and also Inhibits Infective Viral Particle Formation by Dysregulation of Ubiquitin-Proteasome System". *J Neuroimmune Pharmacol* 4 (3): 328–37. doi:10.1007/s11481-009-9158-2.PMID 19434500.

Mishra, MK. and Basu, A. June 2008. "Minocycline neuroprotects, reduces microglial activation, inhibits caspase 3 induction, and viral replication following Japanese encephalitis". *J. Neurochem.* 105 (5): 1582–95.doi:10.1111/j.1471-4159.2008.05238.x. PMID 1820854

Mishra, MK., Dutta, K., Saheb, SK. and Basu, A. December 2009. "Understanding the molecular mechanism of blood–brain barrier damage in an experimental model of Japanese encephalitis: correlation with minocycline administration as a therapeutic agent". *Neurochem Int* 55(8): 717–23. doi:10.1016/j.neuint.2009.07.006.PMID 19628016.

http://www.who.int/biologicals/areas/vaccines/jap_encephalitis/en/

Chatterjee, S., Chattopadhay, D., Bhattacharya, MK. And Mukherjee, B. "serosurveillance of Japanese encephalitis in children in several districts of West Bengal, India", 2004, 1-4

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