22

Systems Thinking: Prevention and Control of Japanese Encephalitis - "The Plague of the Orient"

Kaliyaperumal Karunamoorthi[1,2]
[1]*Unit of Medical Entomology & Vector Control, College of Public Health and Medical Sciences, Jimma University,*
[2]*Research & Development Centre, Bharathiar University, Tamil Nadu*
[1]*Ethiopia*
[2]*India*

1. Introduction

Insect-transmitted diseases impose enormous burden on the world's population in terms of loss of life (millions of death per year) and morbidity. These diseases are also responsible for huge economic losses, both in terms of health-care costs and lost productivity, mostly in countries that can least afford them (Jacobs-Lorena & Anthony, 2002) and, contribute significantly to disease burden, death, poverty, and social debility in the tropical countries (Jang *et al.,* 2002). In particular, developing countries are the foremost sufferer and the major victims of several vector-borne diseases (Karunamoorthi & Sabesan, 2010). More specifically, mosquitoes are the vectors of the dreadful diseases affecting mankind. World Health Organization (WHO) has declared mosquitoes as "the public enemy number one" as they are predominantly responsible for the transmission of various dreadful diseases, such as malaria, filariasis, dengue, yellow fever, and Japanese encephalitis.

1.1 Global public health impact of Japanese encephalitis (JE)

JE is one of the most dreaded mosquito-borne viral encephalitis known to afflict humans and is the leading cause of viral encephalitis (inflammation of the brain) all through the world especially in large parts of Asia with temperate and subtropical or tropical climate (Sabesan *et al.,* 2008). Encephalitis is an infection on the membrane around the brain and spinal cord and is commonly known as **"brain fever"** with high case fatality (Igarashi, 1992a). In Southeast Asia, the incidence of JE appears to be increasing, probably as a result of a steady rise in population density, deforestation, and increasing irrigation of agricultural areas (Igarashi, 1992b).

JE affects predominantly school-age children and is greatly feared because of its high lethality and frequency of permanent neurologic sequelae. Today, approximately 3 billion people are living under the current JE-endemic region (Dutta *et al.,* 2010). The estimated annual incidence and mortality rates are 30,000–50,000 and 10,000, respectively, where as the

estimated global burden of JE in 2002 was 709,000 disability-adjusted life years lost (Keiser *et al.,* 2005).

JE outbreaks occur frequently in 14 Asian countries. However, the lack of reporting system and poor diagnostic tools available for JE limits the appropriate estimation of cases as on date. The use of vaccine is restricted to certain situations only, and no standard formulation is available yet (Sabesan, 2003). Nearly half of the survivors suffer from severe neuropsychiatric sequelae (Dutta *et al.,* 2010). In addition, the social prognosis for handicapped survivors of JE is often poor in developing countries.

2. The historical background of Japanese encephalitis virus (JEV)

From the 1870s, recurring epidemics of encephalitis have been reported from the islands of Japan, especially during the summer season, with major outbreaks occurring every 10 years. This summer encephalitis was termed as type B encephalitis, to differentiate from von Economo's encephalitis lethargica. The name type B was later dropped and in 1935 the Nakayama strain of Japanese encephalitis virus (JEV) was isolated from the brain of a fatal case (Solomon *et al.,* 2000). In just six weeks in 1924, there were more than 6000 cases and 3000 deaths (Solomon, 2006). The virus was later classified as a member of the genus Flavivirus (family Flaviviridae) named after the prototype Yellow fever virus (Latin; flavi = yellow). The genus consisted of over 70 other closely related virus species (Dutta *et al.,* 2010).

The mode of transmission by mosquito vector was elucidated only 25 years after the recognition of JEV (Tiroumourougane *et al.,* 2002). The origins of JEV are uncertain, but phylogenetic comparisons with other flaviviruses suggest that it has evolved from an African ancestral virus, perhaps as recently as a few centuries ago (Gould, 2002) and evolved into its present form in the Indonesia–Malaysia region (Solomon *et al.,* 2003a).

3. Epidemiology

Because of its prevalence and mortality JE is a major public health problem in endemic–epidemic regions. Acute encephalitis occurs in about 1 to 20 cases per 1000 infections, leading to death in 25% of the cases and producing serious neurological lesions in 30% (Burke & Leake, 1988). Children and young adults are most susceptible (Solomon, 1997). The peak transmission period is in summer (from May to October), corresponding with the rainy season and the proliferation of mosquitoes (Halstead, 1992). In endemic zones the percentage of JE antibodies among local resident increases with age. However, during an epidemic outbreak in a previously unaffected region both adults and children are equally susceptible (Umenai *et al.,* 1985). JE is primarily found in South East Asian countries (see Fig. 1). Three epidemiological regions can be distinguished as follows (Rhodain, 1996);

- **The endemic region** made up of southern India, southern Vietnam, southern Thailand, the Philippines, Malaysia and Indonesia. In these regions mosquitoes are more often attracted by birds and pigs where human cases are rare.
- **The intermediary subtropical region** which includes northern India, Nepal, North and Central Burma, northern Thailand, northern Vietnam, southern China and Bangladesh. Transmission is permanent and of low intensity; however, it increases to higher levels

during the rainy season (between April and October). Epidemics in contrast, are severe and concentrated among children.

- **The temperate epidemic region**, spanning northern China, Korea, Japan, Taiwan and the southern extremities of Russia. Transmission is variable coupled with environmental temperature. In winter, mosquitoes are inactive but huge epidemics can be seen in summer and autumn. The geographical area of this disease is showing a trend towards expansion. Postulated explanations are migration of birds, certain irrigation projects, animal smuggling and global warming. Development of rice plantations is theoretically foreseeable in other regions (Pakistan, Afghanistan, Nile Valley, Madagascar and Oriental Africa) creating a favorable environment for further vector proliferation (Rhodain, 1996).

3.1 The geographical distribution of JE

At present, the geographical distribution of JE ranges from Japan, maritime Siberia and the Republic of Korea in the North, to most parts of China and the Philippines in the East, Papua New Guinea in the South, and India and Nepal in the West (see Fig. 1) (Broom *et al.*, 2003). JE is now an emerging viral disease having international importance as it is invading the previously non-endemic areas too. From Asia, it has stretched to Papua New Guinea and Torres Strait of northern Australia (Hanna *et al.*, 1996; Mackenzie *et al.*, 1997). Recent outbreaks of JE have been reported southward in Australia, and westward in Pakistan (Solomon *et al.*, 2000). In recent decades, JE has gradually spread to previously non-affected Asian regions. The reasons for this increased geographic distribution are uncertain, but may include population shifts, and changes in agricultural practices, animal husbandry, migratory bird patterns, and movement of vector mosquitoes to wider areas (Halstead & Jacobson, 2003).

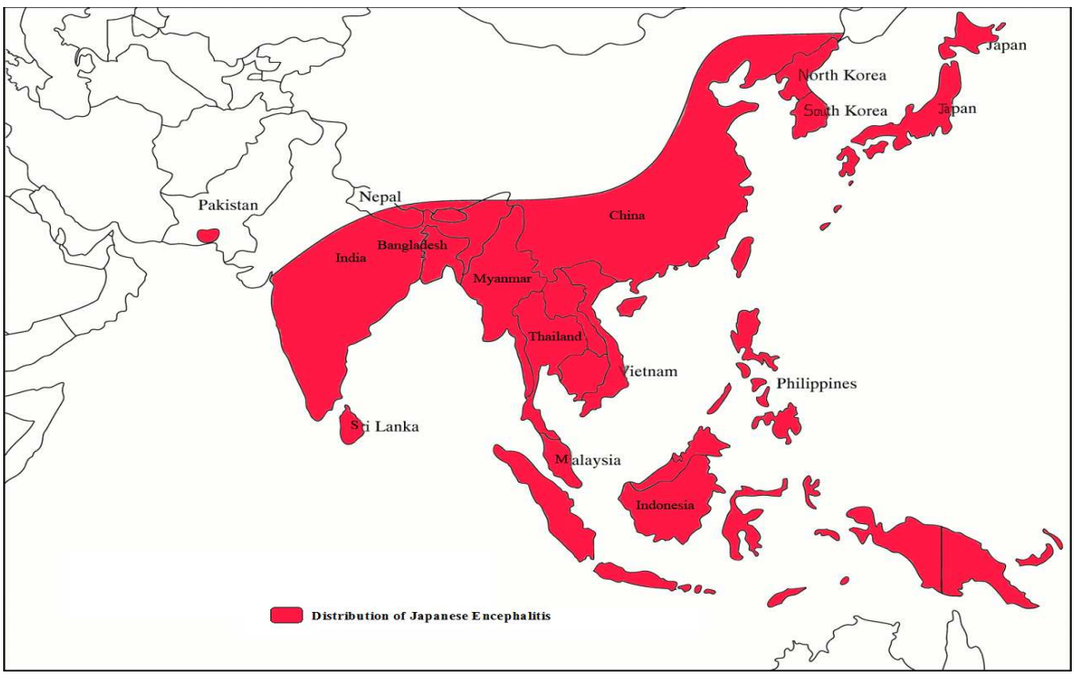


Fig. 1. Map showing the distribution of Japanese Encephalitis

3.2 The causative agent - Japanese encephalitis virus (JEV)

JE virus, is the most common documented cause of viral encephalitis in Asia, and potentially ranks next to the Human Immunodeficiency Virus (HIV) as the most common cause of viral encephalitis in the world (Tsai, 1994). The virus is able to replicate within the salivary glands of the mosquitoes. Mature JE virions remain entrapped in intracellular vacuoles and are later released into the apical cavity of salivary gland cells through the fusion of these vacuoles with the apical plasma membrane. This process is associated with primary re-synthesis of saliva in mosquitoes following blood feeding activity. Another type of shedding involves virus particles, either singly or in mass, being released directly through the apical plasma membrane (Takahashi & Suzuki, 1979).

3.3 Enzootic cycle of JEV

JEV is an arbovirus transmitted in an enzootic cycle involving birds, particularly wading ardeids, such as herons and egrets. Pigs can become infected and act as amplifying hosts. Many mosquito species are potential vectors, but Culex species such as *Culex tritaeniorhynchus* and *C. vishnui,* which breed in rice paddies and other dirty water, are especially important. Humans become infected when they are bitten by infected mosquitoes, but since they have transient and low-level viremia, they are "dead-end" hosts that do not normally transmit virus (Fig. 2).

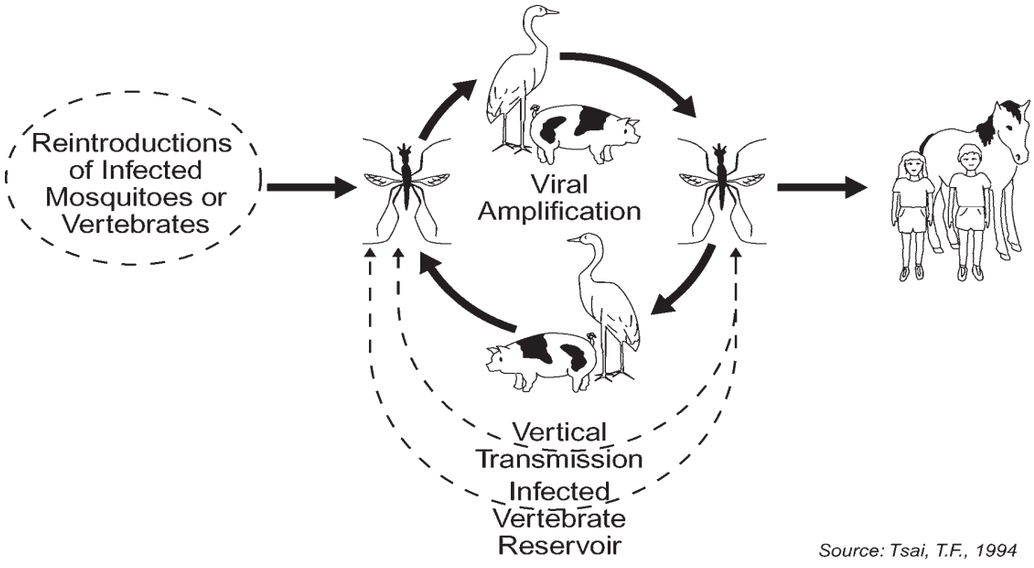


Fig. 2. The transmission cycle of JE

3.3.1 Vector mosquitoes

JE vector mosquitoes are zoophilic, feeding primarily on animal and wild birds and human beings are not considered as a reservoir for viral transmission. It is feeds most often in the outdoors, with the peak biting times after sunset and again after midnight (Fischer *et al.*, 2008). Female mosquitoes get infected after feeding on a viraemic host and can transmit the virus to other hosts after an extrensic incubation period of 9 to 12 days. Man to man transmission has not been documented. The mosquitoes remain infected for life. The

average life period of a mosquito is about 21 days and undergoes three gonotrophic cycle (WHO, 2006).

Human infections are mainly transmitted by *Culex tritaeniorrhynchus* Giles, which is the principal vector of JE in India and South East Asian countries (Suman *et al.,* 2008). The female specimens are infective 9–10 days after having taken the viraemic blood meal, having undergone three gonotropic cycles (Gajanana *et al.,* 1997). Other culicine mosquitoes that can transmit JE include *Cx. bitaeniorhyncus, Cx. epidesmus, Cx. fuscocephala, Cx. gelidus, Cx. pseudovishnui, Cx. sitiens, Cx. vishnui* and *Cx. whitmorei* (Sehgal & Dutta, 2003). The JE incidence, however, varies from country to country; the highest occurrence is found in the rice-growing areas of the country. From this, one may surmise an ecological connection with the irrigation facilities and paddy cultivation (Rajagopalan & Work, 1969).

3.3.2 The pig

Mosquitoes pick the virus from the pigs (which are supposed to be the major reservoir of the virus) and transfer it to humans (Singh, 2007). Pigs with high and prolonged viraemias, are often common in endemic countries, and are generally reared in open and unroofed pigpens, which are located near houses (Mishra *et al.,* 1984; Solomon *et al.,* 2000). In different parts of India, 12 to 44 percent of pig population has been found to be positive for JE antibodies particularly in JE endemic areas (WHO, 2006).

3.3.3 The human, cattle and birds

The presence of JE antibodies in the sera of birds belonging to different species have indicated that *Ardeola grayii* (pond heron) and *Bubulcus ibis* (cattle egret) play a definite role in maintenance of JE virus in nature (WHO, 2006). Humans, goats, cattle and horses are considered to be the dead-end hosts (Reuben *et al.,* 1992). For example, in the Thanjavur district, India, an area with extensive rice agriculture, a very low JE incidence has been reported. This has been explained by high cattle to pig ratio (400:1) (Vijayarani & Gajanana, 2000). In rice-growing villages without herons, seroconversion rates in children aged 0–5 and 6–15 years were 0% and 5%, respectively. In ecologically-similar villages with herons, the corresponding rates were 50% and 56%, respectively (Mani *et al.,* 1991).

4. Clinical manifestations

The disease is characterized by a wide range of presentations, as both the symptoms and the clinical course can differ broadly among patients (Solomon, 1997). On average, only 1 in 300 cases produce clinical symptoms (WHO, 1998). The first signs of infection appear after an incubation period between 6 and 14 days. It usually starts with a fever above 38°C, chills, muscle pain and meningitis-type headaches accompanied by vomiting. The initial presentation in children usually begins with gastrointestinal symptoms: nausea, vomiting and abdominal pains similar to those found in an acute abdominal syndrome. These non-specific signs can continue for 2 to 4 days. However, the patient's state deteriorates rapidly. A progressive decline in alertness takes place eventually leading to deepening coma. Convulsions are experienced by 85% of subjects (Kumar *et al.,* 1990).

The meningeal syndrome predominates with painful neck stiffness. Motor paralyses including hemiplegia and tetraplegia may also be present. Signs of extra pyramidal

involvement, including tremor, rigidity, and abnormal movements are observed in around 30% of the patients (Kumar *et al.,* 1994). Severe clinical cases are likely to have life-long neurological sequelae. Mostly children and young adults are affected (Solomon *et al.,* 2000; Tsai, 2000; Halstead & Jacobson, 2003). Presence of one clinical case in the community suggests that 300 to 1000 people have been infected (WHO, 2006).

5. Laboratory diagnosis

The diagnosis of JE viral infection should be made within an epidemiological context (Endy & Nisalak, 2002). During epidemic outbreaks, a febrile meningeal syndrome should be considered for JE above any other diagnostic consideration. In endemic regions, other arbo-viruses should be investigated when symptoms of viral encephalitis are present, especially in children (Diagana *et al.,* 2007). Nowadays, confirmation of JE virus infection depends mostly on serologic assays such as IgM antibody detection by enzyme-linked immunosorbent assays (ELISA) (Mathur *et al.,* 1990; Shope & Meegan, 1997).

5.1 Detection/isolation of antigen/virus

- Demonstration of viral antigen in the autopsied brain tissue by the fluorescent antibody test.
- Isolation and identification of the virus from CSF, occasionally from peripheral blood (within 3 to 4 days after onset of symptoms) or autopsied brain tissue.

5.2 Detection of antibody

- The diagnosis of JE is supported by serological tests. The tests include detection of IgM antibodies which appear after the first week of onset of symptoms and are detectable for one to three months after the acute episode.
- IgG antibodies indicate previous infection and are useful for conducting seroepidemiological studies to determine the extent of silent infection and immunity levels in the local population.
- The detection of antibodies to JE virus can be done routinely by Haemagglutination Inhibition Test (HI) test to demonstrate fourfold rise in total antibodies and IgM Capture ELISA test for demonstration of IgM antibodies.
- Confirmation of the diagnosis of JE must be based on multiple criteria including clinical, biological, europhysiologic and cerebral imaging findings (Diagana *et al.,* 2007).

6. Approaches for prevention and control of JE

Environmental degradation, socio-economic decline, rapid population movements, migratory birds' movement and the concomitant effects of global warming are contributing to changing pattern of morbidity and mortality and posing serious challenge to public health. Japanese encephalitis remains as major cause of viral encephalitis in Asia, imposing a significant burden on poor rural families. It is a disease of public health importance due to its epidemic potential and high case fatality rate. Even, if patients survive, complications may lead to lifelong sequelae. Therefore the epidemic form of the disease can be minimized by applying the effective control or prevention measures in order to save the lives especially

young children. The strategy for prevention and control of JE includes the following avenues;

1. Surveillance
2. Vector control
3. Personal Protection Interventions
4. Immunization
5. Case management
6. Health education and training
7. Epidemic preparedness and response

6.1 Surveillance

The component of JE surveillance consists of three major areas: (1) Clinical/syndromic surveillance through PHC system for early diagnosis and proper management of JE patients. (2) Vector surveillance in JE prone areas for monitoring vector behaviour and population build up for timely implementation of intervention methods (3) Sero-surveillance to delineate high risk population groups and to monitor JE specific antibodies in sentinel animals or birds as an indication of increasing viral activity (WHO, 2006).

6.2 Vector control intervention strategies

Vector control remains to be the most generally effective measure to prevent/interrupt the disease transmission and is therefore one of the basic technical elements of the vector-borne disease control programme. Currently the following strategies are mainly implemented in order to control the JE vectors and eventually to minimize the disease burden among the rural poor community, despite of their limitations.

6.2.1 Environmental management control strategies

Alternate wet and dry irrigation (AWDI)

Traditionally, flooded rice fields have been the ideal breeding place for several mosquito species, including those that transmit JE. An important feature of this technique involves the alternate wetting and drying of paddy fields, which in turn curtails the life cycle development of the mosquito from larvae and pupae to adult (Keiser *et al.,* 2005). In order to achieve a significant reduction of mosquito larvae, AWDI (also termed intermittent irrigation) has to be applied during the entire cropping season and should cover all rice fields. This method is particularly feasible in places where control of the water supply and drainage is possible, hence where soil and climatic conditions are suitable (Mogi, 1988).

In China, large-scale application of the AWDI technique has been held responsible for significant reductions of rice field breeding vectors and malaria. Growing water shortages in many areas create an incentive to better control of irrigation water. AWDI is also one such strategy (Keiser *et al.,* 2005). A study found that the AWDI has reduced the immature stages of *Cx. tritaeniorhynchus* by 14–91% in rice fields and adult population by 55–70%. The crop yield was examined in two trials and increases between 4 and 13% were observed in AWDI rice fields (Lu-Baulin, 1988). The effect of this method on the incidence of JE has to be investigated (Keiser *et al.,* 2005).

Limitations

- The potential of AWDI is, however, limited in areas where there is a threat of insufficient resources to re-flood the fields and where farmers perceive a risk of reduced yields by letting their fields dry out.

6.2.2 Biological control strategies

Biological control refers to the introduction or manipulation of organisms to suppress vector populations. A wide range of organisms helps to regulate mosquito populations naturally through predation, parasitism and competition (Chandra *et al.,* 2008). Concern about the threat of strong forms of insecticide resistance (Hargreaves *et al.,* 2000) has stimulated renewed interest in alternative control methods including biological control and biopesticides. The best known is the use of *Bacillus thuringiensis* var. *israelensis* (*Bti*) and *B. sphaericus* and, another biocontrol method, the use of larvivorous fish in appropriate water bodies, have been used in mosquito control for over 100 years (Bay, 1967).

6.2.2.1 Larvivorous fish as a biological agent

Recognizing the high larvivorous potential of the fish species *Gambusia` affinis,* it has widely been used to control the immature stages of various vector mosquitoes. Other fish species include *Tilapia* spp., *Poecilia reticulata or Cyprinidae* (Lacey & Lacey, 1990). After stocking rice fields with 1–10 natural predator fish perm^2, larval populations of *Cx. tritaeniorrhynchus* were reduced by 55.2–87.8% (Kim *et al.,* 1994). Larvivorous fish cannot be applied in rice fields, where irregular irrigation is practiced. It should also be noted that predator populations are strongly influenced by the temperature, rice growth, vegetation, use of pesticides or chemical pollutants (Lacey & Lacey, 1990).

In addition, recent research has shown that ovipositing mosquitoes may move to other breeding sites in response to the stocking of rice fields with predatory fish (Angelon & Petranka, 2002). Furthermore, the introduction of exotic predators such as *Gambusia* might displace the native fish populations to reduce their natural value, as being observed in Japanese rice fields (Wada, 1988). Therefore, the compatibility of the chosen fish with local fauna and flora is of high importance (Lacey & Lacey, 1990).

6.2.2.2 Bacteria as biocides

The larvicidal activity of the spore forming bacteria *B. sphaericus* and *B. thuringiensis israelensis* were discovered in 1965 and 1976, respectively (Mittal, 2003). In Tamil Nadu, India, the application of 4.3 kg/ha of a microgel droplet formulation of *B. sphaericus* 1593M resulted in a 44–79% reduction of early instar and 82–100% reduction of late instar culicinae larvae (*Cx. fuscanus, Cx. pseudovishnui* and *Cx. tritaeniorhynchus*) for at least 5 weeks (Sundararaj & Reuben, 1991). Similarly, up to 95–98% of *Cx. tritaeniorhynchus* larvae were reduced in three other field sites evaluating *B. sphaericus or B. thuringiensis* formulations (Balaraman *et al.,* 1983; Rhee *et al.,* 1983; Kramer, 1984). However, the larvicidal activity did not persist in these rice fields beyond a couple of days; in the Republic of Korea the residual effect of *B. thuringiensis* H-14 was found to last only for 24 h (Rhee *et al.,* 1983).

Limitations

- The application of larvicides may not be an appropriate control strategy in terms of cost effectiveness because of the widespread breeding reservoirs of *Cx. tritaeniorrhynchus.*

- Biocides are not only expensive but also their effectiveness can withstand only for a few days. Therefore, it requires frequent and repeated applications at least at the end of every week.
- *In general, biocides are* effective against mosquito larvae but cannot control the pupal stage.

6.2.2.3 Invertebrate predators

Invertebrate predators, i.e. *Coleoptera*, *Hemiptera* or *Odonata*, though less common than the use of fish, are also known to substantially reduce mosquito larval populations in rice fields. However, they are highly sensitive to temperature, presence of vertebrates, growth of rice and chemical pollutants (Lacey & Lacey, 1990). In India, the presence of notonectids was negatively associated with the larval abundance of *Cx. pseudovishnui, Cx. tritaeniorrhynchus* and *Cx. vishnui* (Sunish & Reuben, 2002).

6.2.2.4 Fungi

Fungi that have been studied extensively for their potential as biological mosquito control agents include *Coelomomyces* spp. and *Lagenidium giganteum*. The former have been investigated with regard to how they impact the development of JE vectors in China (Keiser *et al*., 2005). Field observations showed a strong effect of the fungus *Coelomomyces indica* on *Cx. tritaeniorhynchus*, as infected larvae were unable to develop into adults (Liu & Hsu, 1982). However, fungi have not been applied for biological control of JE vectors on a large scale so far, as practical problems, for example their production, have yet to be solved (Lacey & Lacey, 1990).

6.2.2.5 Algae

The floating water fern Azolla (Salviniales: Azollaceae) contains a symbiont nitrogen-fixing cyanobacteria, *Anabaena azollae* Strasburger, and is regarded as a source of organic fertilizer for rice cultivation (Lumpkin & Plucknett, 1980). Azolla multiplies rapidly and forms a thick surface mat which has been shown, in laboratory studies, to interfere with oviposition of mosquitoes as well as adult emergence from pupae (Amerasinghe & Kulasooriya, 1986; Rajendran & Reuben, 1988).

In China, the major vectors breeding in rice-fields say, *Cx. tritaeniorhynchus* and *An. sinensis* are found to have significant reductions of larvae in paddy fields where rice was cultivated in association with *Azolla pinnata* (Anonymous, 1986). In Tamil Nadu, India, application of the floating water fern *Azolla microphylla* greatly reduced immature mosquito populations. However, the infestation of the rice field with Azolla was difficult to achieve and 80 percent coverage by *Azolla* was accomplished only 13–14 days after rice transplantation, limiting its wider use as a biological mosquito control agent (Rajendran & Reuben, 1991).

6.2.3 Chemical control strategies

Indoor residual spraying (IRS)

IRS remains to be the most widely used vector control intervention. Its application has been thoroughly standardized and there are clear specifications for suitable equipment and insecticides. As the main effect of IRS is the killing of mosquitoes entering houses and resting on sprayed surfaces, it is not useful for the control of vectors which tend to rest outdoors, although it may be effective against outdoor biting mosquitoes which enter houses for resting after feeding.

IRS is relatively ineffective against the highly exophilic vectors, not only because of the resting habits of the vectors, but also because of the mobility of settlements, which remain unreported and inaccessible. In southern Henan province, China, DDT residual indoor spraying had no effect on the incidence of JE, but it was greatly reduced after the introduction of pyrethroid-impregnated bed nets. Only a small effect on outdoor biting densities of Culex tritaeniorhyncus was found, although the number of mosquitoes resting inside bed nets decreased markedly after the introduction of bed net impregnation (Luo *et al.,* 1994). The recent evidence also shows that IRS is ineffective against JE vectors (Sabesan *et al.,* 2008).

6.3 Personal protection interventions

6.3.1 Insecticide Treated Mosquito Nets (ITMNs)

The insecticidal treatment of nets adds a chemical barrier to the often imperfect physical barrier provided by the net and thus, improves its effectiveness in personal protection. ITMNs are easy to use devices for preventing mosquito -borne diseases such as JE, malaria, etc. The absence of reliable surveillance data, difficulties of vaccine production, and shortages and high costs of the commercial vaccine are thought to restrict the implementation of vaccine programs, especially in low-income countries (WHO, 1998; Monath, 2002). The interventional strategy using ITMNs will have an important epidemiological implication in bringing down the JEV activity in the pig-rearing communities without disturbing their social custom of rearing pigs, which they have been carrying on for ages. As well, this may provide a cost-effective way to reduce JEV transmission and supplement the relatively high cost of vaccines (Dutta et al., 2011).

Limitations

- Majority of the JE vectors have shown the bimodal feeding activity (the peak biting times after sunset and again after midnight) and people often stay outdoors at dusk hours during when ITNs may not be useful to reduce the man-vector contact.
- In addition, the JE vectors feeds most often in the outdoors and therefore, in these above circumstances deployment of ITNs may not be a feasible strategy and therefore, the application of repellents could be a useful alternative intervention measures.

6.3.2 Repellent

Repellents are playing key role in order to reduce the man-vector contact and eventually to reduce the vector-borne diseases (Karunamoorthi & Sabesan, 2010). Protection against insect bites is best achieved by avoiding infested habitats, wearing protective clothing, and applying insect repellent (Curtis, 1992; Fradin, 2001). Although insecticide-treated bed nets protect against mosquitoes and malaria in many parts of the world, people may contract disease in the early evening before they retire to the confines of the net, since exposure to malaria vectors and nuisance mosquitoes starts in the early evening (Maxwell *et al.,* 1998).

Insect repellents are extremely useful to the travelers, who visit for a short-span of time in the JE endemic areas. The main advantage is that the repellents are relatively cheap, highly effective and can be applied as a short-term measure.

Limitations

- Personal protection through mosquito coils and indigenous materials (oils,smokes, etc.) is widely practiced in agricultural communities but is of doubtful effectiveness in terms of protection against transmission, although it often provides some relief from the "nuisance" aspect in situations of high mosquito (including vector) biting densities. Commercial repellents are generally too expensive for poor farmer communities.

6.3.2.1 Plant –based repellents

Plants have been used since ancient times to repel/kill bloodsucking insects in the human history and even now, in many parts of the world people are using plant substances to repel/kill the mosquitoes and other blood-sucking insects (Karunamoorthi *et al.,* 2008). At the moment repellent of plants origin have been receiving massive attention due to their environmental and user friendly nature as they are easily available, accessible and affordable (Karunamoorthi *et al.,* 2009).

6.3.2.2 Plant-based products against JE vector mosquitoes

Petroleum ether (60–80°C) extracts of the leaves of *Vitex negundo* have acted as a promising repellent against *Cx. tritaeniorrhynchus* (Karunamoorthi *et al.,* 2008). Recent study results reveal that the hexane extracts of *A. marmelos* and *A. paniculata* can serve as potential repellent, ovicidal, and oviposition deterrent against Japanese encephalitis vector, *Cx. tritaeniorrhynchus* (Elango *et al.,* 2010). Globally, numerous studies evidently suggest that the traditionally used plant-based insect repellents are promising and could potentially contain many vector-borne diseases in particular JE (Karunamoorthi *et al.,* 2008; 2010).

6.3.2.3 Removal of Pig farming

The removal of the pigs acting as amplification hosts appears to have stopped the circulation of JEV in Singapore. The incidence of reported serological confirmed cases of JEV has been declining since pig farming has been eliminated in the country. The incidence has dropped from 101 cases during 1977–1984 to 15 cases for 1985–1992 (Anonymous, 1994).

Limitations

- This intervention strategy may not be feasible in the resource-poor settings, where majority of the people largely consider pigs as a source of income and desire food.

6.4 Immunization

Immunization provides a reasonable and practical way to control JEs, but the selection of target populations may present a problem in countries where JE outbreaks cannot be clearly defined in terms of places of infection and affected age groups. However, immunization is recommended for protecting populations where JE virus attacks are highly probable. Monitoring of JE activity will help to identify populations at the risk of exposure who can then be given a booster immunization (Umenai *et al.,* 1985).

6.4.1 Types of vaccine

Three types of vaccine against the Japanese encephalitis virus is presently licensed to be produced and administered worldwide. The inactivated mouse-brain derived JE vaccine is available on the international market. Primary hamster kidney (PHK) cell derived

inactivated and live attenuated JE vaccines are widely used in China. A comparison between the inactivated mouse-brain derived vaccine and the PHK-derived live-attenuated vaccine shows a similar immunogenicity (84-100% seroconversion after 3 doses vs. 94-100% seroconversion after 2 doses), efficacy (91% with two doses vs. 97% with two doses) and with incidence of minor side effects. The inactivated JE vaccine was associated with rare incidence of severe allergic reactions and neurological complications (Mori & Siegel, 2000).

6.4.2 Dosage and route of administration

Dosage schedules differ for endemic and non-endemic regions. Children in endemic areas may need fewer doses because of previous immunity or subsequent exposures to flaviviruses that boost up antibody levels (ACIP, 1993). In endemic areas, the inactivated Biken vaccine is administered subcutaneously in two 0.5-mL doses between one to four weeks apart. Primary vaccination varies from the age of 18 months in Thailand to 3 years in Japan. Boosters are often given one year after primary vaccination and at intervals of 3 years thereafter (Tsai, 1994). In non-endemic regions, the Advisory Committee on Immunization Practices (ACIP) recommends a three-dose regimen on days 0, 7, and 30 with a booster given after one year and every three years thereafter (ACIP, 1993). Normal administration in China consists of a 0.5-mL dose at years of 1 and 2. A final booster is given in year six (Hennessy *et al.,* 1996).

6.4.3 Pig vaccination

Live attenuated JE vaccine has been developed in Japan primarily for immunization of pigs to prevent still births. In the Republic of Korea live attenuated JE vaccine using baby hamster kidney cells has also been developed and used for the vaccination of pigs (Umenai *et al.,* 1985). Immunization of pigs may be attempted to control JE epidemics because it has been established that these animals, after vaccination with the live vaccine, showed no viraemia on exposure to infected mosquitoes. The immunized pigs must have therefore been unable to "amplify" the virus transmission. However, all investigators engaged in this project pointed out that effective immunization was not easy because of the high turnover in the pig population so that individual pigs might escape being immunized (Umenai *et al.,* 1985). Vaccination of pigs has been used but has not been shown to consistently reduce mosquito and human infections and is not cost-effective in most settings. However, moving pigs away from human habitats also makes sense (Solomon, 2006).

6.4.4 WHO position on JE vaccination

Considering the current existence of safe and effective vaccines at a relatively low cost for wide scale use, the WHO advises the integration of the JE vaccine into the WHO immunization initiative in regions where this disease constitutes a public health risk. Therefore, systematic vaccination campaigns (in the form of 'vaccination days') are needed to allow the progressive integration of JE vaccination into the WHO immunization initiative. Despite a few cases of encephalomyelitis reported in children after having received the Mouse Brain-derived JE Vaccine, the WHO is considering using it in its immunization campaign since the benefits far outweigh the risks. Because of the availability and simplicity of use, the attenuated live vaccine based on the SA 14-14-2 strain offers an interesting alternative (Diagana *et al.,* 2007).

Limitations

- It should be mentioned that JE vaccine is not always available because the cost of commercial vaccines is still too high for use in large-scale vaccination. Work on the development of second generation (genetically engineered) vaccines is in progress.

6.5 Case management

6.5.1 Treatment

At present there are no established antiviral treatments against JE. *Interferon alpha* was the most promising drug in small open-label trials, but it failed to affect the outcome in children with JE (Solomon *et al.,* 2003). Though we are handicapped by the non-availability of a specific drug against JE, mortality and morbidity can be decreased appreciably by control and treatment of factors causing secondary deterioration such as raised intracranial pressure and convulsions. The value of this approach has been documented in traumatic coma (Ghajar & Hariri , 1992).

6.6 Health education

- Simple Information on JE - cause, transmission and prevention of mosquito bites.
- Community action in reducing mosquito breeding places by filling pools, weekly drainage of accumulated water, lowering of water levels in rice fields etc.
- National guidelines for diagnosis, management and prevention of JE - for programme managers and health professionals.

The people of JE-prone areas can be motivated through information, education and communication (IEC) activities/awareness campaigns on the dreadful disease. Using ITMNs for self-protection and protecting pigs from mosquito bites can efficiently check the JEV transmission in the JE prone areas. (Dutta *et al.,* 2011).

6.7 Epidemic preparedness and response

- Immediately notify government authorities by phone, fax or email.
- A team of investigators consisting of clinicians, epidemiologists, entomologists etc. should be immediately sent to the affected site, to take action.
- The team should be provided with proper information on collection of specimens;
  - Stool samples – for isolation of enterovirus
  - Blood or serum on the first three days of the illness – for detection or isolation of virus
  - Paired serum samples at an interval of at least 10 days – for antibody detection.
  - Cerebral Spinal Fluid (CSF) – for virus isolation and antibody tests
  - In case of deaths – tissue samples of brain and liver.

Conclusively, the JE disease control programmes have been focusing on the three major areas; (1) mosquito control, (2) amplifying host (pig) control, and (3) vaccination. However, neither mosquito control nor amplifying host (pig) control has been proven (in India) to be an effective measure to control JE, as they are carried out mostly after the outbreaks. Spraying the entire epidemic prone area is time consuming, expensive, and it is difficult to cover all mosquito habitats. Moreover, it is discouraged on account of environmental pollution. Since the biting activity of JE mosquitoes is at dusk, use of bed nets at night is likely to be ineffective and it shall not be the best solution for JE control. Segregating,

slaughtering, or vaccinating pigs is economically not feasible and also difficult in other logistic angles. Since other animals, like birds also act as amplifying hosts just pig elimination shall not override JE (Sabesan *et al.,* 2008).

It seems that there is compelling evidence that human immunization is effective for containing the JE epidemics. Since the epidemic in man appears to follow epizootics which coincide when the vector density shoots up in the anticipated epidemic districts, feasibility of JE vaccination has to be considered as a preventive measure. In such situations, identifying the risk area and determining the target population to be immunized are crucial. Therefore, a routine JE immunization may be initiated in all areas identified for the risk of epidemics (Sabesan *et al.,* 2008).

One cannot affirm with or advocate the universal appropriate JE preventive/control measures. However, selecting the community oriented appropriate control strategy is extremely essential to minimize the mortality and morbidity due to JE. There are a number of effective intervention strategies currently available and therefore, one can select/prefer, the most appropriate intervention based on the local availability, accessibility, and affordability from the following recommendations;

- Changes in agricultural and animal husbandry practices
- Creating awareness by effective health education campaign through electronic media viz., printed pamphlet, news papers, radio and television
- Avoiding the outdoor stay at dusk hours during the main transmission period
- Intermittent irrigation system, if possible.
- Application of repellents during dusk hours in order to reduce the man-vector contact
- Consistent deployment of ITNs
- Immunization to the vulnerable section of the society especially for children (<15 years).
- Rational use of appropriate insecticide in the resting sites of mosquitoes, viz; domestic and peri-domestic areas, cattle sheds, pigsties, chicken coops etc. to suppress the vector density in risky areas prior to transmission (Sabesan et al., 2008).
- Promoting the use of bio-control agents (fishes/'Azolla', etc) and organic fertilizers ('neem' cakes) to reduce the mosquito immatures (Sabesan *et al.,* 2008).
- Monitoring viral activity in vector mosquitoes and reservoir animals in order to supplement with the information on vector abundance to predict the risk of transmission (Sabesan *et al.,* 2008).

7. Acknowledgement

I am greatly indebted to Dr. K. Ilango M.Sc., Ph.D., Scientist, Zoological Survey of India, Chennai, India and Dr. S. Sabesan M.Sc., Ph.D., Scientist, Vector Control Research Center, Ponidcherry, India for their constant encouragement and support. I would like to thank Mrs Melita Prakash for her sincere assistance. My last but not the least heartfelt thanks go to my colleagues of our Department of Environmental Health Science, College of Public Health and Medicine, Jimma University, Jimma, Ethiopia, for their kind support and cooperation.

8. References

Amerasinghe, F.P. & Kulasooriya, S.A. (1986). Azolla vs mosquitoes: some experiments with *Culex quinquefasciatics*. *MIRCEN Journal*, Vol. 2, pp. 355-363.

Angelon, K.A. & Petranka, J.W. (2002). Chemicals of predatory mosquitofish (*Gambusia affinis*) influence selection of oviposition site by *Culex* mosquitoes. *Journal of Chemical Ecology*, Vol. 28, pp. 797–806.

Anonymous. (1986). Azolla study initiated in China. WHO/FAO/UNDP PEEM Newsletter No. 15,3-4.

Anonymous. (1994). Epidemiological News Bulletin 20 (5) (published by the Ministry of the Environment, Singapore).

Balaraman, K., Balasubramanian, M. & Jambulingam, P. (1983). Field trial of *Bacillus thuringiensis* H-14 (VCRC B-17) against Culex and Anopheles larvae. *Indian Journal of Medical Research*, Vol. 77, pp. 38-43.

Bay, E.C. (1967). Mosquito control by fish: A present-day appraisal. WHO Chronicle, Vol. 21, pp. 415-423.

Broom, A.K., Smith, D.W., Hall, R.A., Johansen, C.A. & Mackenzie, J.S. (2003). Arbovirus infections. In: Cook, G., Zumla, A. (Eds.), Manson's Tropical Diseases, 21st ed. Saunders, London, pp. 725–764.

Burke, D.S. & Leake, C.J. (1988). Japanese encephalitis. In: Monath TP, editor. The Arboviroses: Epidemiology and ecology, vol. 3. Boca Raton FL: CRC Press, pp. 63-93.

Centers for Disease Control and Prevention. "Inactivated Japanese encephalitis virus vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP)." MMWR. 42: RR1-15, 8 January 1993.

Chandra, G., Bhattacharjee, I., Chatterjee, S.N., & Ghosh A. (2008). Mosquito control by larvivorous fish. *Indian Journal of Medical Research*, Vol. 127, pp. 13-27.

Curtis, C.F. (1992). Personal protection methods against vectors of disease. *Review of Medical and Veterinary Entomology*, Vol. 80, pp. 543–553.

Diagana, M., Preux, P. & Dumas M. (2007) Japanese encephalitis revisited. *Journal of the Neurological Sciences,* Vol. 262, pp. 165-170.

Dutta, K., Rangarajan, P.N., Vrati S., & Anirban Basu, A. (2010) Japanese encephalitis: pathogenesis, prophylactics and therapeutics. *Current Scien*ce, Vol. 98(3), pp. 326-334.

Dutta, P., Khan, S.A., Khan, A.M., Borah, J., Sarmah, C.K. & Mahanta, J. (2011).The Effect of Insecticide-Treated Mosquito Nets (ITMNs) on Japanese Encephalitis Virus Seroconversion in Pigs and Humans. *American Journal of Tropical Medicine and Hygie*ne, Vol. 84(3), pp. 466-472.

Elango, G., Rahuman, A.A., Bagavan, A., Kamaraj, C., Zahir, A.A., Rajakumar, G., Marimuthu, S.& Santhoshkumar, T. (2010). Efficacy of botanical extracts against Japanese encephalitis vector, *Culex tritaeniorrhynchus*. *Parasitology Research*, Vol. 106, pp. 481-492.

Endy, T.P. & Nisalak, A. (2002). Japanese encephalitis virus: ecology and epidemiology. In: Mackenzie JS, Barrett ADT, Deubel V, editors. Japanese Encephalitis and West Nile Viruses. Berlin: Springer-Verlag; pp. 12-48.

Fischer, M,, Hills, S., Staples, E., Johnson, B., Yaich, M., & Solomon, T. (2008). Japanese encephalitis prevention and control: advances, challenges, and new initiatives. Scheld WM , Hammer SM , Hughes JM , eds. Emerging Infections 8 . Washington, DC : American Society for Microbiology Press, pp. 93-124 .

Fradin, M.S. (2001). Protection from blood-feeding arthropods. In:Auerbach PS (ed) Wilderness Medicine, 4th edn. Mosby, St.Louis, pp 754–768.

Gajanana, A., Rajendran, R., Samuel, P.P., Thenmozhi, V., Tsai, T.F., Kimura-Kuroda, J. & Reuben, R. (1997). Japanese encephalitis in South Arcot district, Tamil Nadu India: a three-year longitudinal study of vector abundance and infection frequency. *Journal of Medical Entomology*, Vo. 34, pp. 651–659.

Ghajar, J. & Hariri, R.J. (1992). Management of pediatric head injury. *Pediatric Clinics of North America*, Vol. 39, pp. 1093-1012.

Gould, E.A. (2002) Evolution of the Japanese serological group viruses. In Current Topics in Microbiology and Immunology: Japanese Encephalitis and West Nile Virus Infections (eds Mackenzie, J. S., Barrett, A. D. and Deubel, V.), Springer-Verlag, Berlin, pp. 391-404.

Halstead, S.B. & Jacobson, J. (2003). Japanese encephalitis. Advances in Virus Research, Vo. 61, pp. 103-138.

Halstead, S.B. (1992). Arboviroses of the Pacific and Southeast Asia. In: Feigin V, Cherry JD, editors. Textbook of pediatric infectious diseases. 3rd edition. Philadelphia: WB Saunders; pp. 1468–1475.

Hanna, J.N., Ritchie, S.A., Phillips, D.A., Shield, J., Bailey, M.C., Mackenzie, J.S., Poidinger, M., McCall, B.J. & Mills, P.J. (1996). An outbreak of Japanese encephalitis in the Torres Strait Australia. *Medical Journal of Australia*, 1996; 165, 256–260.

Hargreaves, K., Koekemoer, L.L., Brooke, B.D., Hunt, R.H., Mthembu, J. & Coetzee, M. (2000). *Anopheles funestus* resistant to pyrethroid insecticides in South Africa. *Medical and Veterinary Entomology*, Vol. 14, pp. 181-189.

Hennessy, S., Zhengle, L., Tsai, T.F., et al. (1996). "Effectiveness of live-attenuated Japanese encephalitis vaccine (SA14-14-2): a case control study." *Lancet*, Vo. 347, pp. 1583-1586.

Igarashi, A. (1992a). Epidemiology and control of Japanese encephalitis. *World Health Statistics Quarterly*, Vol. 45, pp. 299-304.

Igarashi, A. (1992b). Japanese encephalitis: virus, infection, and control. Kurstak E, ed. Control of Virus Diseases. Second edition. New York: Marcel Dekker, pp. 309-342.

Jacobs-lorena, M., & James, A.A. (2002). Genetic modification of insects of medical importance: past, present and future. Report t of the Scientific Working Group on Insect Vectors and Human Health, TDR/SWG/VEC/03.1 P68-73.

Jang, Y.S., Kim, M.K., Ahn, Y.J., & Lee, H.S. (2002). Larvicidal activity of Brazilian plants against *Aedes aegypti* and *Culex pipiens* pallens (Diptera: Culicidae). *Agricultural Chemistry Biotechnology*, Vol. 45(3), pp. 131-134.

Karunamoorthi, K. & Sabesan, S. (2010). Laboratory evaluation of dimethyl phthalate treated wristbands against three predominant mosquito (Diptera: Culicidae) vectors of disease. *European Review of Medical and Pharmacological Science*, Vol. 14(5), pp. 443-448.

Karunamoorthi, K., Ilango, K. & Endale, A. (2009). Ethnobotanical survey of knowledge and usage custom of traditional insect/mosquito repellent plants among the Ethiopian Oromo ethnic group. *Journal of Ethnopharmacology*, Vol. 125(2), pp. 224-229.

Karunamoorthi, K., Ilango, K. & Murugan, K. (2010) Laboratory evaluation of traditionally used plant-based insect repellent against the malaria vector *Anopheles arabiensis* Patton (Diptera: Culicidae). *Parasitology Research*, Vol. 106(5), pp. 1217-1223.

Karunamoorthi, K., Ramanujam, S. & Rathinasamy, R. (2008). Evaluation of leaf extracts of *Vitex negundo* L. (Family: Verbenaceae) against larvae of *Culex tritaeniorhynchus* and repellent activity on adult vector mosquitoes. *Parasitology Research*, Vol. 103, pp. 545-550.

Keiser, J., Maltese, M.F., Erlanger, T.E., Bos, R., Tanner , M., Singer, B.H. & J¨urg Utzinger, J. (2005). Effect of irrigated rice agriculture on Japanese encephalitis, including challenges and opportunities for integrated vector management. *Acta Tropica*, Vol. 95, pp. 40-57.

Kim, H.C., Kim, M.S. & Yu, H.S. (1994). Biological control of vector mosquitoes by the use of fish predators *Moroco oxycephalus* and *Misgurnus anguillicaudatus* in the laboratory and semi-field rice paddy. *Korean Journal of Entomology*, Vol. 24, pp. 269-284.

Kramer,V. (1984). Evaluation of *Bacillus sphaericus* & *B. thuringie*nsis H-14 for mosquito control in rice fields. *Indian Journal of Medical Research*, Vol. 80, pp. 642-648.

Kumar, R., Mathur, A., Kumar, A., Sharma, S., Chakraborty, S. & Chaturvedi, V.C. (1990). Clinical features and prognosis indicators of Japanese encephalitis in children in Lucknow (India). *Indian Journal of Medical Research,* Vol. 91, pp. 321-327.

Kumar, R., Selvan, S.A., Sharma, S., Mathur, A., Misra, P.K., Singh, G.K., et al. (1994). Clinical predictors of Japanese encephalitis. *Neuroepidemiology*, Vol. 13, pp. 97-102.

Lacey, L.A. & Lacey, C.M. (1990). The medical importance of Riceland mosquitoes and their control using alternatives to chemical insecticides. *Journal of American Mosquito Control Association*, Vol. 2 (Suppl.), pp. 1-93.

Liu, S.L. & Hsu,Y.C. (1982). Effect of the fungus *Coelomomyces indica* on the viability of *Culex tritaeniorhynchus* larvae. Kun Chong Xue Bao, Vol. 25, pp. 409-412.

Lu Bao-Lin, (1988). The effect of Azolla on mosquito breeding. *Parasitology Today*, Vol. 4, pp. 328-329.

Lumpkin. T.A. & Plucknett, D.L. (1980). Azolla: botany, physiology and use as a green manure. *Economic Botany*, Vol. 34, pp. 111-153.

Luo, D., Yoa, R., Song, J., Huo, H. & Wang, Z. (1994). The effect of DDT spraying and bed nets impregnated with pyrethroid insecticide on the incidence of Japanese encephalitis virus infection. *Transactions of Royal Society of Tropical Medicine and Hygiene*, Vol. 88(6), pp. 629-631.

Mackenzie, J.S., Poidinger, M., Phillips, D., Johansen, C.A., Hall, R.A., Hanna, J., et al., (1997). Emergence of Japanese encephalitis virus in the Australasian region. In: Saluzzo JF, Dodet B, editor. Factors in the emergence of arboviruses diseases. Paris: Elsevier; pp. 191-201.

Mani, T.R., Rao, C.V., Rajendran, R., Devaputra, M., Prasanna, Y., Hanumaiah, Gajanana, A. & Reuben, R. (1991). Surveillance for Japanese encephalitis in villages near Madurai, Tamil Nadu, India. *Transactions of Royal Society of Tropical Medicine and Hygiene*, Vol. 85, pp. 287-291.

Mathur, A., Kumar, R., Sharma, S., Kulshreshtha, R., Kumar, A. & Chaturvedi, U.C. (1990). Rapid diagnosis of Japanese encephalitis by immunofluorescenct examination of cerebrospinal fluid. *Indian Journal of Medical Research*, Vol. 91, pp. 1-4.

Maxwell, C.A., Wakibara, J., Tho, S. & Curtis, C.F. (1998). Malaria infective biting at different hours of the night. *Medical and Veterinary Entomology*, Vol. 12, pp. 325-327.

Mishra, A.C., Jacob, P.G., Ramanujam, S., Bhat, H.R. & Pavri, K.M. (1983). Mosquito vectors of Japanese encephalitis epidemic in Mandya district (India). *Indian Journal of Medical Research*, Vol. 80, pp. 377-389.

Mittal, P.K. (2003). Biolarvicides in vector control: challenges and prospects. *Journal of Vector Borne Diseases*, Vol. 40, pp. 20-32.

Mogi, M., 1988. Water management in rice cultivation and its relation to mosquito production in Japan. In: Vector Borne Disease Control in Humans Through Rice Agro-ecosystem Management. International Rice Research Institute in collaboration with the WHO/FAO/UNEP Panel of Experts, pp. 101–109.

Monath, T.P. (2002). Japanese encephalitis vaccines: current vaccines and future prospects. *Current Topic on Microbiology and Immunology*, Vol. 267, pp. 105- 138.

Mori, M.C. & Siegel, R. (2000). Live attenuated Japanese encephalitis (SA14-14-2) vaccine: The best alternative? June 3, 2000. http://www.stanford.edu/~siegelr/mori.html. accessed on 9th February 2011.

Rajagopalan, P.K. & Work , T.H. (1969). An Analysis of mosquito collections with special reference to the incidence and prevalence of '*Culex vishnui* Complex' in the Japanese encephalitis infected localities of North Arcot District, Madras State, India, from December 1955 through December 1957. *Indian Journal of Medical Research*, Vol. 57, pp. 1409-1419.

Rajendran, R. & Reuben, R. (1988). Laboratory evaluation of the water fern *Azolla pinnata*, for mosquito control. *Journal of Biological Control*, Vol. 2, pp. 114- 116.

Rajendran, R. & Reuben, R. (1991). Evaluation of the water fern *Azolla microphylla* for mosquito population management in the rice land agro-ecosystem of South India. *Medical and Veterinary Entomology*, Vol. 5, pp. 299-310.

Reuben, R., Thenmozhi, V., Samuel, P.P., Gajanana, A. & Mani, T.R. (1992). Mosquito blood feeding patterns as a factor in the epidemiology of Japanese encephalitis in Southern India. *American Journal of Tropical Medicine and Hygiene*, Vol. 46, pp. 654-663.

Rhee, H.I., Shim, J.C., Kim, C.L. & Lee, W.J. (1983). Small scale field trial with Bacillus thuringiensis israelensis H-14 for control of the vector mosquito (*Culex tritaeniorhynchus*) larvae in rice fields. *Korean Journal of Entomology*, Vol. 13, pp. 39-46.

Rhodain, F. (1996). Données récentes sur l'épidémiologie de l'encéphalite japonaise. *Bulletin of the National Academy of Medicine*, Vol. 180, pp. 1325-1340.

Sabesan, S. (2003). Forecasting mosquito abundance to prevent Japanese encephalitis. *Current Science*, Vol. 84, No. 9, pp. 1172-1173.

Sabesan, S., Konuganti, H.R. & Vanamail, P. (2008). Spatial Delimitation, Forecasting and Control of Japanese Encephalitis: India – A Case Study. *The Open Parasitology Journal*, Vol. 2, pp. 59-63.

Sehgal, A. & Dutta, A.K. (2003). Changing perspectives in Japanese encephalitis in India. *Tropical Doctor*, Vol. 33, pp. 131-134.

Shope, R.E. & Meegan, J.M. (1997). Arboviruses. Evans AS, Kaslow RA, eds. Viral Infections of Humans. Fourth edition. New York: Plenum, 151−183.

Singh, A. (2007). Menace of Japanese encephalitis in rural areas of eastern Uttar Pradesh. *Current Science*, Vol. 93, No. 12, pp 1649.

Solomon, T. (1997). Viral encephalitis in Southeast Asia. *Neurological Infections and Epidemiology*, Vol. 2, pp. 191-199.

Solomon, T. (2006). Control of Japanese encephalitis – within our grasp? *New England Journal of Medicine*, Vol. 355, pp. 869-871.

Solomon, T., Dung, N. M., Kneen, R., Gainsborough, M., Vaughn, D. W. & Khanh, V. T. (2000). Japanese encephalitis. *Journal of Neurology, Neurosurgery and Psy*chiatry, Vol. 68, pp. 405-415.

Solomon, T., Dung, N.M., Wills, B., Kneen, R., Gainsborough, M., Diet, T.V., Thuy, T.T., Loan, H.T., Khanh, V.C., Vaughn, D.W., White, N.J. & Farrar, J.J. (2003). Interferon alfa-2a in Japanese encephalitis: a randomised double-blind placebo-controlled trial. *Lancet*, Vol. 361, pp. 821-826.

Solomon, T., Ni, H., Beasley, D.W.C., Ekkelenkamp, M., Cardosa, M.J. & Barrett, A.D. (2003a). Origin and evolution of Japanese Encephalitis Virus in Southeast Asia. *Journal of Virology*, Vol. 5, pp. 3091-3098.

Suman, D.S., Shrivastava, A.R., Parashar, B.D., Pant, S.C., Agrawal, O.P. & Prakash, S. (2008). Scanning electron microscopic studies on egg surface morphology and morphometrics of Culex tritaeniorrhynchus and Culex quinquefasciatus (Diptera: Culicidae). *Parasitology Research*, Vol. 104, pp. 173-176.

Sundararaj, R. & Reuben, R. (1991). Evaluation of a microgel droplet formulation of Bacillus sphaericus 1593M (Biocide-S) for control of mosquito larvae in rice fields in Southern India. *Journal of American Mosquito Control Association*, Vol. 7, pp. 556-559.

Sunish, I.P. & Reuben, R. (2002). Factors influencing the abundance of Japanese encephalitis vectors in ricefields in India-II Biotic. *Medical and Veterinary Entomology*, Vol. 16, pp. 1-9.

Takahashi, M. & Suzuki, K. (1979). Japanese encephalitis virus in mosquito salivary glands. *American Journal of Tropical Medicine and Hygiene*, Vol. 28, pp. 122-135.

Tiroumourougane, S.V., Raghava, P. & Srinivasan, S. (2002). Japanese viral encephalitis. *Postgraduate Medical Journal*, Vol. 78, pp. 205-215.

Tsai, T.F, Yu. (1994). "Japanese encephalitis vaccines." Vaccines.[edited by] Stanley A. Plotkin, Edward A. Mortimer, Jr. Philadelphia : W.B. Saunders Co., 1994.

Tsai, T.F. (2000). New initiatives for the control of Japanese encephalitis by vaccination: minutes of a WHO/CVI meeting, Bangkok, Thailand, 13–15 October 1998. Vaccine 18 (Suppl. 2), 1-25.

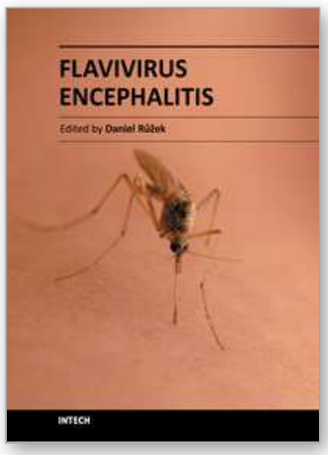
Umenai, T., Krzysko, R., Bektimirov, T.A. & Assaad, F.A. (1985). Japanese encephalitis: current worldwide status. *Bulletin of World Health Organizat*ion, Vol. 63(4), pp. 625-631.

Vijayarani, H. & Gajanana, A. (2000). Low rate of Japanese encephalitis infection in rural children in Thanjavur district (Tamil Nadu), an area with extensive paddy cultivation. *Indian Journal of Medical Research*, Vol. 111, pp. 212-214.

Wada, Y. (1988). Strategies for control of Japanese encephalitis in rice production systems in developing countries. In: Vector Borne Disease Control in Humans Through Rice Agroecosystem Management. International Rice Research Institute in collaboration with the WHO/FAO/UNEP Panel of Experts, pp. 153–160.

WHO. (1998). Japanese encephalitis vaccine. WHO position paper. *Weekly Epidemiology Reco*rd, Vol. 73, pp. 337-344.

WHO. (2006). Guidelines for Prevention and Control of Japanese Encephalitis. http://whoindia.healthrepository.org/handle/123456789/187. accessed on 9th February 2011.



Flavivirus Encephalitis

Edited by Dr. Daniel Ruzek

ISBN 978-953-307-669-0
Hard cover, 478 pages
Publisher InTech
Published online 30, September, 2011
Published in print edition September, 2011

Encephalitis is an inflammation of the brain tissue associated with clinical evidence of brain dysfunction. The disease is of high public health importance worldwide due to its high morbidity and mortality. Flaviviruses, such as tick-borne encephalitis virus, Japanese encephalitis virus, Murray Valley encephalitis virus, or St. Louis encephalitis virus, represent important causative agents of encephalitis in humans in various parts of the world. The book Flavivirus Encephalitis provides the most recent information about selected aspects associated with encephalitic flaviviruses. The book contains chapters that cover a wide spectrum of subjects including flavivirus biology, virus-host interactions, role of vectors in disease epidemiology, neurological dengue, and West Nile encephalitis. Special attention is paid to tick-borne encephalitis and Japanese encephalitis viruses. The book uniquely combines up-to-date reviews with cutting-edge original research data, and provides a condensed source of information for clinicians, virologists, pathologists, immunologists, as well as for students of medicine or life sciences.

INTECH
open science | open minds

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
www.intechopen.com

InTech China
Unit 405, Office Block, Hotel Equatorial Shanghai
No.65, Yan An Road (West), Shanghai, 200040, China
中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
Phone: +86-21-62489820
Fax: +86-21-62489821

IntechOpen