"Japanese encephalitis – the plague of the east that was"

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Abstract

The causes and magnitude of the Japanese encephalitis (JE) epidemics in Asia is described. Results of entomological biological, ecological and seroepidemiological studies of JE for the Asian region are shown. The history of JE in Sri Lanka is outlined and the causes of the major epidemic of JE in 1987 are described. The clinical experience obtained by treating 134 patients with JE in the Polonnaruwa base hospital and Colombo North Teaching Hospital, Ragama are described. Three clearly defined, distinct stages of the illness are shown.

Unusual clinical manifestations not described elsewhere are highlighted. The presence of viral lymphocytes in the CSF is shown as a diagnostic marker of JE. The high incidence of permanent impairment of higher function in children who survive J. E. is described. The impact of JE vaccination in Sri Lanka is shown and the need for expanding it and its introduction to the primary immunizing programme is suggested.

Introduction

Japanese encephalitis (J.E.) is a severe neurological disease with widespread inflammation of the brain. Clinically it is characterized by fever, headache and impaired consciousness. It is a major health problem and a dreaded disease due to its high case fatality rate and grave neurological sequlae.

The clinical features of the disease was described as early as 1871 in Japan. However, the causative agent, the Japanese encephalitis virus an arbovirus, was not isolated until 1935[1].

The J.E. virus is an RNA virus and belongs to the family Flaviviridae. Under the electro microscope it appears as a spherical, enveloped structure, measuring 50n m. In the centre lies the RNA genome containing the C(core protein) surrounded by the M(membrane protein) and the outer E (envelop protein).

The J.E. virus is transmitted to man through the bite of Culex tritaenorhyncus or related mosquito species. These mosquito larvae breed in paddy fields and then preferentially bite the amplifier vertebrate host, pig or cattle. The virus multiplies very efficiently in pigs to produce sufficient viraemia to infect other vectors and act as amplifier host in J.E. transmission. Humans are considered "dead end hosts" because of negligible viraemia and inability of further viral transmission.

Pathogenesis

Following infected mosquito bite, the J.E. virus enters the venous circulation traverses the heart and reaches the cerebral vasculature. However, in the majority of cases, the virus does not cross the blood brain barriers and only produces features of viraemia such as fever, arthralgia and myalgia.

In the small proportion of cases, the J.E. virus crosses the blood brain barrier and enters the substance of the brain. In such instances, all the features of an acute encephalitic illness occur.

Japanese encephalitis is a disease which clearly demonstrates the "iceberg phenomenon". Seroepidemilogical studies have shown that only one out of 300 patients, infected by J.E. virus develop an encephalitic illness. The majority remain as inapparent infection and can be detected only by antibody surveys[2].

J.E. in Asia

Today, Japanese encephalitis is prevalent in the Asia monsoon region in East, South East and South Asia. This area extends from Japan and Korea in East Asia to China, Hong Kong, Vietnam, Thailand and Burma in South East Asia to India, Nepal and Sri Lanka in South Asia[3].

In Japan, Japanese encephalitis has been a major public health problem until 1966. Since then, the number of cases has decreased considerably as a result of mass vaccination. In Korea, no officially recognized cases have been reported after 1983, probably the result of mass vaccination.

In Thailand, Vietnam, China and India large outbreaks have been reported at regular intervals and encephalitis apparently continues to spread.

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Interaction of 3 factors have resulted in the high incidence of Japanese encephalitis in Asia.

1. Weather pattern

All countries plagued by J.E. are situated in the "Asia monsoon region" and receive very high rainfall from November to January each year from North - East monsoonal winds. This is invariably followed by epidemics of J.E. in this region.

2. Rice cultivation

Rice is the staple diet of people in the Orient. The paddy fields, watered by monsoonal rains, provide excellent breeding grounds for mosquito larvae.

3. Pig breeding

This is a common form of animal husbandry carried out in Asian countries due to the relative low cost of rearing and feeding pigs and the rapid turnover of the pig population.

Entomological studies of Japanese encephalitis in Asia.

From the below table it is evident that C. vishnui was the major Culex vector in India[4]. C. traitaeno-rhyncus was responsible for J.E. epidemics in Burma[5], Sri Lanka[6]. C. gelidus was the main vector of the Indonesian epidemic of 1987[7].

Seroepidemiological studies in the community and in animals –

Seroepidemiological studies have been done to determine the major vertebrate amplifier host and the prevalence of J.E. antibody in the community after major epidemics of J.E.

Seroepidemiological studies reveal that pig is the main amplifier host of J.E. transmission in, Burma[5], Sri Lanka[6] and Thailand[7]. In India[4], cattle were the more important amplifier host followed by pig and birds (pigeons and herons).

Japanese encephalitis in Sri Lanka

Encephalitis has been prevalent in Sri Lanka for many decades. During the last 25 years commencing 1968, an average if approximately 1000 cases have been admitted to government hospitals each year with a mean case fatality rate of 28%[8]. The first isolation of J.E. virus in Sri Lanka was from a patient in Panadura in 1968.

The Japanese encephalitis epidemic of Sri Lanka in 1987 to 1988

A major epidemic of J.E. occurred in the North Central Province (particularly in Anuradhapura district) between November, 1987 and January 1988. During this epidemic, 787 cases of J.E. were reported with deaths, giving a case fatality rate of 19.8%.

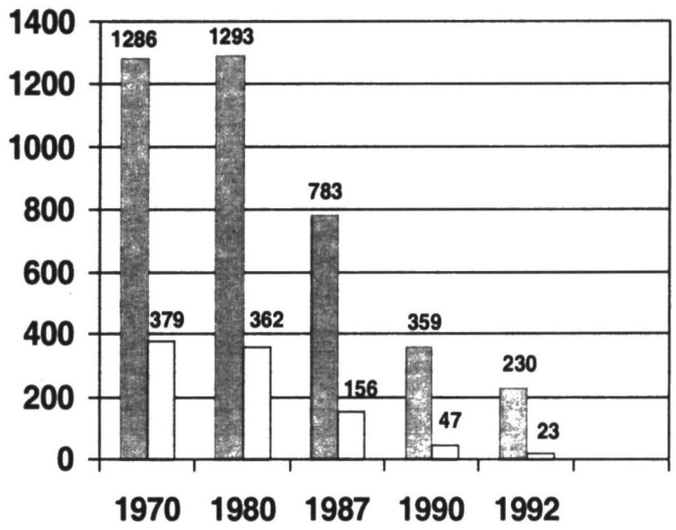
Table 1. Vectors Japanese encephalitis/culex species indentified during epidemics

Country	*Period*	*Cx. tritaenorhyncus*	*Cx. gelidus*	*Cx. vishnui*	*Cx. fuscocephala*
India	1985-86	+	+	44.5%	-+
Thailand	1987-88	+	+	-	-
Indonisia	1987-88	+	+++	-	-
Burma	1982-83	++	+	-	-
Sri Lanka	1987-88	46%	35%	+	-

Table 2. Results of seroepidemiological studies J.E. antibody prevalence %

Country	*Year*	*Pig*	*Cattle*	*Pigeon*	*Heron*
India (Nagaland)	1985-86	34	52	21	22
Indonisia	1986-87	65	-	-	-
Thailand	1987-88	54	-	-	-
Burma	1982-83	52	-	-	-

Table 3.



JAPANESE ENCEPHALITIS IN SRI LANKA INCIDENCE & CASE FATALITY

Table 4. Incidence of Japanese encephalitis

Country	*Year*	*No of cases*	*% of children*	*Adults*
Sri Lanka	1985	535	45	55%
	1986	339	58	42%
	1987	789	30	70%
	1988	207	45	55%
India (Karanataka)	1986	280	68	32%
India (Nagaland)	1985	50	100	
Thailand	1984	59	100	

Anuradhapura had the majority of cases (409) followed by Kurunegalle (116) Puttalam (101) and Polonnaruwa (68). J.E. was also reported from Vavuniya, Trincomalee and Batticaloa[8,9].

An unusual feature of the J.E. epidemic from 1985 onwards has been the high incidence of infection among the adult population. This is in contrast to the previous epidemics where predominantly children have been affected. The higher incidence of J.E. in the adult population in the last epidemic in Sri Lanka was due to the mass colonization under the Mahaweli project.

Causes of the epidemic of J.E. in the North Central Province of Sri Lanka in 1987-88.

(1) Colonization into "System H" and "System B" of the Mahaweli in the Anuradhapura and Polonnaruwa districts.

People who were previously living in the hill country (non endemic areas for J.E.) who lost their traditional homelands in the hill country were settled within system H and system B of the Mahaweli, within the Anuradhapura and Polonnaruwa districts respectively

– both highly endemic areas for Japanese encephalitis transmission.

Colonization occurred systematically from 1982, onwards, but reached a peak in 1985 when nearly 1000 family units were settled in these districts.

This led to a mixture of the old colonists who had lived in these areas for years and developed natural immunity to J.E. (as a results of exposure during previous epidemics) with the new colonists who came from non endemic areas with absolutely no immunity to J.E. this, sudden influx of 1000 vulnerable families into a highly endemic area resulted in a major epidemic especially among adults in 1987.

(2) Increase in vector density –

Increase in number of breeding sites resulted from vast areas of the Mahaweli being opened up for rice cultivation. Following the North – East monsoon these water filled, still paddy fields provide excellent breeding ground for Culex mosquitoes.

Furthermore, jungle clearing and the establishment of human settlements and creation of seepage pools provided further vector breeding grounds.

(3) Pig breeding

This new form of animal husbandry was unfortunately introduced into both system H+ B of the Mahaweli. Pig breeding provided the "Amplifier host" to complete the life cycle of J.E. in close proximity to paddy fields where Culex larvae bred.

Epidemiological studies done by Peiris et al have clearly shown the correlation of porcine infection with human disease in Anuradhapura[10].

Clinical experience with J.E. patients

Clinical experience obtained by treating 134 cases of J.E. is outlined below. This group comprised 32 children and 58 adults treated at base hospital Polonnaruwa, between 1986 and 1988 and 44 adults treated at the Colombo North General Hospital, Ragama between 1989 and 1991.

Clinical features of J.E.

Three stages of the illness are clearly defined.

I. The prodromal stage : 2-5 days
II. The acute encephalitis stage : 4-8 days
III. The convalescent stage : 1-3 days

The presenting features of J.E. at the time of admission were – fever (100%), headache (77%), abnormal behavior (72%) and convulsions (22%). The fever was of remittent type, very high and failed to respond to paracetamol and cold sponging. The fever subsided at the end of the acute encephalitic stage spontaneously or continued until the patient died. Headache was intense and association with irritability, vomiting and photophobia.

Abnormal behavior, though not described in epidemics of J.E. elsewhere, was frequently encountered and was considered to be a common early pointer to possible diagnosis of J.E. Abnormal behavior varied from vacant stare, mask like facies, poor attention span and lethargy.

The neurological state observed in hospital varied from confusion (60%), drowsiness (45%), coma (29%), to delirium (15%) and violence and aggression (1%).

The other unusual neurological manifestations seen in a small proportion of patients were muscle twitching, cerebellar ataxia, floppy neck and mixed dysphasia. Floppy neck was associated with detrimental effect on speech, deglutition and progress of physiotherapy.

The commonest motor abnormality observed among patients with J.E. in Sri Lanka was spastic quadraparesis (45%), followed by flaccidity (22%) and palatal palsy (20%). The surveys done in Thailand, India and Burma also indicate spasticity as the major neurological abnormality[11,12,13].

Diagnosis of J.E.

The clinical diagnosis of J.E. was confirmed by the examination of cerebro spinal fluid (CSF) in all patients without evidence of papilloedema for presence of antibody IgM by the ELISA test. (enzyme linked immunosorbent assay)

Paired sera were examined for rising antibody titre IgG in 52% of samples, by the haemagglutination inhibition test (HAI).

Close examination of CSF showed viral lymphocytes. These cells were larger than the normal with large nuclei filling the cytoplasm but showing open chromatin network. These viral lymphocytes have not been highlighted in other epidemics of J.E. in Asia.

The results of ELISA test in the CSF and HAI in the sera in Sri Lanka are comparable to the Indian survey.

The moderate positivity of ELISA may be due to the early examination of CSF before. IgM antibody

response occurred in the CSF. This early examination was done as most patients presented early to hospital due to the wide publicity given to J.E. by the media.

Treatment of J.E.

Patients received symptomatic treatment with paracetamol, mannitol and anticonvulsants when indicated. Benzyl-penicillin and chloramphenicol IV were given until a diagnosis of bacterial meningitis was excluded. Patients with incidental malaria were treated with appropriate anti malarial therapy. Incidental chest and urine infections were treated with appropriate antibiotics.

Poor prognostic features were –

1. Persistent high fever lasting more than 10 days.
2. status epilepticus – lasting more than 02 days.
3. Prolonged coma – more than 05 days.
4. Persistent bradycardia despite high.temperature.
5. Brain stem encephalitis with – severe decerebrate rigidity.

Outcome – mortality

Out of 90 patients treated for J.E. Polonnaruwa, between 1986 to 1988, there were 18 deaths, giving a mortality of 20%. In the Ragama survey between 1989 and 1991 the mortality rate was 15.9%. The mortality rate for J.E. in Karnataka. India was 28% and Thailand was 17%. Unfortunately, surveys with low case fatality rates are associated with high degree of neurological squelae as indicated below.

Neurological squelae in children

Neurological assessment was carried out at the following stafes of illness.

1) At the time of discharge
2) Six months after epidemic of J.E.
3) Three years after the epidemic of J.E. in 1991.

Out of 52 patients who survived the epidemic of J. E. in 1987, 22 patients (42%) presented at the special follow up clinic held three years after discharge.

Out of 32 children who were treated for J.E. 17 recovered completely, 10 recovered partially and 5 children died.

Out of 10 children who had recovered partially at the time of discharge, five were found to be normal at the three year reassessment.

Among the other 05 patients, there was evidence of impairment of higher function, although gross motor deficits had improved considerably. Impairment of higher mental function included poor attention span, poor control of epilepsy, dyscalculia, dysgraphia and poor sociability.

Among adults who had neurological deficits at the time of discharge, only two patients had residual spasticity. This is in total contrast to the situation in children where the J.E. virus sometimes causes permanent damage to the immature growing brain, leading to deterioration of higher function in 50% of children who recovered partially from J.E.

Table 5. Incidence of Japanese encephalitis

Country	*Period*	*No of cases*	*No of deaths*	*Case fatality rate %*
India (Karanataka)	1986-87	219	61	28
Thailand	1985-87	59	10	17
Sri Lanka				
Polonnaruwa	1986-88	90	18	20
Ragama	1989-91	44	7	15.9
Entire	1987-88	787	157	19.9

Prevention and control of Japanese encephalitis

The importance of prevention of Japanese encephalitis cannot be over emphasized in view of the high case fatality and grave residual neurological deficits.

The control strategy of Japanese encephalitis is based on the natural transmission cycle of Japanese encephalitis. Thus 3 control strategies can be applied.

1) Vector control
2) Immunization of pigs
3) Human immunization

Vector control

Spraying of pesticides is practically unfeasible due to wide area of vector breeding in paddy fields. Concerted fogging with permethrine and spraying of malathion have been carried out so far by the anti malaria campaign.

Pig Immunization

This has been carried out in the major Japanese encephalitic epidemic areas of Anuradhapura, Polonnaruwa and Puttlam since 1988. However, pig immunization is not cost effective due to the rapid turnover of the pig population bred mostly for human consumption and killed within 08 months of birth.

Impact of Japanese encephalitis immunization in Sri Lanka

Immunization commenced in Sri Lanka. in 1988 after the major epidemic of 1987 which caused a case fatality rate of 18.6%. The impact of vaccination in reducing the incidence of J.E. since introduction of J.E. vaccine in Sri Lanka in 1988 is shown below.

Conclusion

Japanese encephalitis is a lethal disease, associated with high mortality and grave neurological sequelae. It is endemic in many areas of Sri Lanka. The persistence of the Japanese encephalitis virus is ensured by the interaction of three main foci of the life cycle.

With economic, social development and population expansion, there is bound to be more agricultural colonization and land utilization in Sri Lanka in the future. This is likely to lead to even larger outbreaks of Japanese encephalitis in the future.

Human immunization is the most reliable control measure for Japanese encephalitis. Today, a safe and effective vaccine is available. Hence I consider that Japanese encephalitis vaccination should be introduced into primary immunization schedule in Sri Lanka.

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