JAPANESE ENCEPHALITIS ; A MAJOR HEALTH PROBLEM IN SRI LANKA

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Introduction

Encephalitis is an inflammation of the brain most commonly due to a viral infection. There are several viruses which can cause encephalitis. Studies done at the MRI show that the Japanese Encephalitis virus is the most important cause and probably accounts for over 80% of cases in Sri Lanka. Rabies is another important cause. Among the other viruses Measles, Mumps, Enteroviruses, Adenoviruses and Herpes simplex in that order, are causes of encephalitis in Sri Lanka.

Japanese Encephalitis (JE) is a serious public health problem with a high mortality, specially in children and old people, in many countries of Asia. The virus was first isolated in Japan in 1935 and the illness it caused was earlier referred to as Japanese B Encephalitis. This was because there was another type of encephalitis which was referred to as Japanese A Encephalitis. However, the latter was found to be identical with Von Economo's disease which was found in other parts of the world, and is not found any longer in Japan, and has been dropped. Therefore, the term Japanese B Encephalitis is no longer used, and this disease is now called Japanese Encephalitis.

The incidence of JE was high in Japan, Korea and China from about 1930 to 1960. A significant reduction was noticed from about 1965 in Japan after the implementation of wide scale immunization with a killed vaccine. With the use of this vaccine there was a drop in the incidence in Korea and Taiwan as well subsequently. However, the incidence in China has continued to remain high. But in the 1970's the incidence of JE has increased in South East Asia particularly in Thailand, Vietnam and Burma.[1] In South Asia too there has been a significant increase - specially in India and Nepal. This increase has been evident in Sri Lanka after 1980 but it was most evident after the 1985/86 epidemic, in the Anuradhapura and Puttalam districts. Most of the cases of JE in all countries occur among children, but no age is exempt.

The Epidemiology

Japanese Encephalitis is an infection caused by a virus belonging to the genus *Flavivirus*. It is closely related to the Dengue viruses which are also present in Sri Lanka. These viruses are transmitted by mosquitoes and therefore referred to as Arboviruses (arthropod-borne viruses).

In nature, the main reservior of JE infection is not human beings but various animals. Of these the most important is the pig, which is considered to be an amplifier host. This is because the virus is found at the highest levels for the longest period (3-7 days) in the blood of the pig. Therefore, a mosquito vector biting a pig has the greatest chance of getting infected.

Research done by us at the Medical Research Institute (MRI) showed that more than 80% of pigs tested in Ragama, Tissamaharama Anuradhapura and Chilaw districts had evidence of past infection. In contrast,

1 T. Umenai., R. Krzysko., A. Bektimirov and F.A. Assaad (1985) Japanese Encephalitis : Current Worldwide Status, Bulletin of World Health Organization, 63(4) : 625-631.

among cattle, goats and dogs only about 30-50% were infected. The figure among birds was much lower. Because virus is found for a shorter period and at lower levels in the other animals, the chance of a mosquito getting infected by them is much lower than from a pig.

Although about 140 species of mosquitoes have been described in Sri Lanka only a few appear to be involved in the transmission of JE. The main vector mosquitoes appear to be *Culex tritaeniorhynchus* and *Culex gelidus*. *Culex fuscocephala* and *Culex pseudovishnui* appear to be vectors of lesser improtance. *Culex gelidus* appears to be more important in the western coastal belt and the suburban areas where they breed in shallow ditches and pools. *Culex tritaeniorhynchus* and the other vectors are found more in rice fields.

Females of these vector mosquito species get infected when they take a blood meal from an infected animal such as a pig. The virus multiplies in the cells of the mosquito, such as the coelomic epithelium, and then reach the salivary glands in about 9-12 days, after which the mosquito becomes infective.

The mosquito vectors prefer to feed on animals and transmit the infection to them. The spill over of infection to humans occurs when the absolute number of infected mosquitoes increases. Thus water logging of rice fields and pools (specially after rains) and the close proximity of these breeding sites to human dwellings promote the transmission to people. JE is therefore mainly a rural disease, though it can occur in the outskirts of towns which are close to rice fields or pools.

The JE virus does not produce any illness in most of the animals infected, with the exception of encephalitis in horses and abortion in pregnant pigs. Studies done in several villages in Sri Lanka by the MRI team suggest that only about one out of 300 to a 1000 infected people develop encephalitis. The others get a minor fever or do not show any illness at all.

Pathological and Clinical Features

In Japanese Encephalitis, nerve cells in the brain are damaged mainly in the mid-brain, cerebral cortex and cerebellum. The anterior horns of the spinal cord may be affected. Blood vessels are dilated with occasional bleeding and there may be lymphocytes and other cells around them. Inflammatory cell infiltration of the brain and meningeal coverings may also occur.

After the virus enters the body following a mosquito bite it travels to the liver, spleen, and some lymph glands where the virus multiplies within the macrophages. The virus is then released into the blood stream after 5-12 days (incubation period) and with this fever occurs. The fever may be accompanied by chills (and shivering), severe headache, malaise and sometimes nausea and vomitting. In many cases the illness does not progress beyond this point and the fever comes down in 3-6 days. In a few, the virus may enter the brain and cause encephalitis.

The fever continues to be high with a relatively slower pulse. The face may take on a Parkinsonian look (dull, staring, mask-like), with thick retarded speech. Neck stiffness is common and muscular rigidity may occur. Altered consciousness (clouding of consciousness, excitement, confusion, disorientation, stuper and coma) generally occurs. Tremors and involuntary movements of various types and incoordination are common. Convulsions (fits) too are common specially in children. Paralysis occurs and may be trivial or extensive. In Anuradhapura, weakness of neck muscles was seen in some cases. Changes in reflexes are not prominent. Sensory changes are difficult to demonstrate because of altered consciousness.

Involvement of other systems, such as the myocardium of the heart can occur.

The case fatality (death rate) usually ranges between 20 and 40% but in some epidemics has exceeded 60%. In the recent (1985/86) Anuradhapura and Chilaw outbreaks it was about 20%. Death usually occurs within 10 days of the onset of illness. Death is due to the results of destruction of nerves cells and swelling of the brain. Patients may die of heart or respiratory failure or during fits.

Other causes of death are complications like pneumonia, urinary infection, lack of fluid and food, and bed sores

due to poor nursing care. The death rate has been reduced in the hospitals by reducing the swelling of the brain through the use of mannitol, preventing fits by suitable drugs, providing adequate food and fluid, and preventing and treating the complications like bacterial infections.

Unfortunately, upto 50% of those who survive have some remaining defects, which may clear-up gradually or even remain for life. These defects may vary from minor emotional or psychiatric disturbances to intellectual deterioration and even to complete paralysis and dementia.

It was not easy to establish the diagnosis of Japanese Encephalitis in a patient upto 1985, as two samples of blood or cerebro-spinal fluid (CSF) collected at a time interval of about 10 days had to be tested for Haemagglutination Inhibition (HI) or neutralizing antibodies. Usually the first sample had no antibody or only low levels, while the second sample had a significantly higher level of antibody. As a result, a diagnosis could only be established in those patients from whom two adequately spaced blood or CSF samples were received.

Isolation of the virus can be done using mice, tissue culture or mosquito inoculation techniques. These are time-consuming and require samples that have been maintained at a low temperature to ensure survival of the virus. It is therefore not a routine diagnostic procedure, but it is important from a point of view of research and control (choice of appropriate vaccine).

Since 1985 the development of the IgM capture Enzyme Linked Immunosorbant Assay (ELISA) by Donald Burke has made it possible to detect specific JE IgM antibody in a single sample of CSF (or blood) and make a definite diagnosis.

History of Japanese Encephalitis in Sri Lanka

The virus was first isolated in Sri Lanka from a human patient by Hermon et al. at the Medical Research Institute in 1968.[2] But its presence was suspected earlier when a child died of encephalitis at the School for the Blind at Mahawewa in June 1960. One of the serum samples sent to the Virus Research Centre at Poona, India was positive for group B arbovirus, probably Japanese Encephalitis.

While encephalitis occurred sporadically throughout the year in most parts of the country, the first major outbreak occurred in the Kurunegala district in 1971. This mainly affected children and in the course of that year 76 cases were admitted to the children's ward at Kurunagala Hospital. There was a high case fatality of 66 deaths and of the 10 who survived 5 had residual neurological deficits. Unfortunately, by the time the Medical Research Institute was informed, it was too late to establish the cause of the outbreak. In 1971 a study was made of encephalitis cases admitted to the Children's Hospital, Colombo and District Hospital, Gampaha.

Of the 31 cases admitted to DH Gampaha, 6 were serologically investigated at the MRI and one was found positive for JE. Out of 50 cases at the Children's Hospital, 4 were serologically investigated but there were no positives.

Thereafter, cases occurred sporadically throughout the island and for the 10 year period 1971 to 1980 there was an average of 1,030 hospital admissions each year for encephalitis with a mean case fatality rate of 38% (range of 25% - 45%). During this period etiological studies done at the MRI on a limited number showed that Japanese Encephalitis is the leading cause, accounting for 43.3%.[3]

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2 Y.E. Hermon., M. Anandarajah. (1974) - Isolation of Japanese Encephalitis virus from the serum of a child in Ceylon. Ceylon Medical Journal, 19.02.93-99.

3 Tissa Vitarana (1982) - Viral Diseases in Sri Lanka. Viral Diseases in South-East Asia and Western Pacific - Ed. John S. Mackenzie, Academic Press, Sydney, 198-204.

A serological survey done by us in 1976 and 1977 in various parts of Sri Lanka indicated that Japanese Encephalitis occurred mainly in certain parts of the country (see Map).[4] These were the Western coastal belt extending from Kalutara in the south upto Puttalam in the north and inland for about 10-15 miles to include Gampaha. Domestic pig rearing is common in this area and 83% of pigs tested had quite high levels of HI and NT antibodies against JE. The other areas affected were those with large rice fields and where wild pigs occur such as the districts of Kurugenala, Anuradhapura, Batticaloa and Tissamaharama. There was some JE activity in the Northern province as well. There was little or no JE in the hill country.

JE Outbreaks

At the beginning of 1985 (January and February), 32 cases of encephalitis were warded at the Anuradhapura Hospital. Of these, 13 were positive for JE by the newly introduced MAC ELISA test for JE specific IgM in the CSF. Two of these were also positive by haemagglutination inhibition (HI) and neutralization (NT) tests.

Commencing in November 1985 and extending to February 1986 there was a major outbreak of JE involving the Anuradhapura and Chilaw districts. In Anuradhapura there were 406 cases of encephalitis with 76 deaths.[5] An unusual feature of this outbreak was that about 50% of cases occurred in the age group 20-50 years and there was a preponderance of male patients. In Chilaw there were 106 cases with 17 deaths, but this followed the classical pattern and mainly affected children.[5]

On the basis of ongoing field research studies it would appear that the factors contributing to the Anuradhapura outbreak were :

1. The increased area of rice cultivation and the excess rain, which led to pooling, leading to an increase of vector mosquito breeding;

2. Encouragement and increase of pig breeding in the area;

3. An increase of non-immune people for example through migration from areas, such as the hill country, where the JE virus is less active.

In the Chilaw area the main contributory factor appears to be the increase of vector mosquitoes, due to the excessive rains, and a build up of susceptible children.

A bigger epidemic of over 600 cases of JE occurred in the Anuradhapura District at the end of 1987 and early 1988.

Impact of Irrigation Schemes such as the Mahaweli

In the Anuradhapura district most cases during the last outbreak occurred in the 'H' area of the Mahaweli Scheme. Studies done in 1985 by a team from the MRI, AMC and AFC showed that there is past and present JE activity in the Mahaweli System 'C' and in the Lunugamwehera Scheme at Tissamaharama.[6] However, the level of JE activity was much lower than in the 'H' area of the Mahaweli.

There is clearly a need to carefully monitor JE virus activity and vector mosquito densities in these irrigation schemes.

Control of JE in Sri Lanka

Immunization of children aged 1-10 years was commenced in the middle of 1988. In the highest risk areas

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4 U.T. Vitarana., M. Kanapathipillai (1977). - Prevalence of Arbovirus Infections in Sri Lanka. Results of a 1976 survey compared with that of 1966. Proc. Sri Lanka Ass. Adv. Sci. 32,7.

5 Vitarana. T., Jayasekera, N., Herath, P., et al. Japanese Encephalitis Outbreak in Sri Lanka ; Association with new irrigation schemes. Virus Diseases in Asia (Thongcharoen and Kurstak ed.) (1988) Mahidol University, Bangkok, 193-196.

6 Tissa Vitarana, Pushpa Herath, Kingsley Kalpage, Nalini Jayasekera, Mervyn Wickramasinghe and Varuni Gunatillake (1985) Study of Mosquito Borne disease in some new irrigation shemes in Sri Lanka - Diseases Aspects. Paper read at seminar organized by IIMI at Digana. 9-13.

i.e. Anuradhapura and Puttalam districts, 2 doses of killed JE vaccine are given at intervals of 2-4 weeks and followed by a booster injection one year later. Studies done by the MRI have shown that the vaccines imported from Japan and Korea are equally effective.[7] The antibody responses in a group of vaccinated children is being followed to determine when a further booster is required. This may be about 3-4 years after the 3rd dose, as is recommended in Japan.

Though it is desirable that all children aged 1-10 years should be immunized in all the endemic areas (or even the whole country) the government finds itself unable to find the money for this. Therefore, the MRI has conducted antibody surveys in the endemic areas and worked out an order of priority according to the JE virus activity in each area. With the available vaccine from 1989 onwards more and more children in the endemic areas are being brought under vaccine cover.

The benefit of this programme is already evident in that the occurrence of JE cases among children has come down to extremely low levels in the vaccinated areas.

Together with this, other control measures are also being implemented. These are vaccination of pigs and water management to reduce vector mosquito breeding. If the water level in the rice fields is lowered to ground level one day in a week then the mosquito larvae and pupae die. While this is possible to do in large irrigation schemes with sufficient stored water, it is not possible in smaller irrigation schemes. Preliminary studies done at the MRI show that fish like guppies, are good feeders on vector mosquito larvae.

Further research is needed to find out how these fish will resist chemicals and poisons used in agriculture. The MRI has planned out such a research programme with the Agricultural Research Centre at Mahalluppallama. A study on the effects of agricultural chemicals on vector mosquito larvae is also planned.

The MRI also has established an early warning system by setting up 10 sentinel study points in the endemic areas. At these points, by regular monitoring it is possible to determine when vector mosquito densities begin to increase. When this occurs, the AMC is informed and they do widespread malathion spraying in surrounding areas around the pig-pens. At this time, health education programmes are intensified so that people will take suitable action to avoid being bitten by the vector mosquitoes which bite at night time, mainly between 6.00 p.m. and 10.00 p.m. and 3.00 a.m. and 6.00 a.m.

It is hoped that through a combination of all these control measures, the incidence of this dreadful disease can be reduced to low levels or if possible eliminated.

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7 Vitarana U.T., Colombage G., Bandaranayake, V., Gunasekera H.D.N., Hettiarachchi L., Peiris L. - Antibody responses following the use of Japanese Encephalitis Vaccine manufactured in Korea and Japan in a sample of Sri Lanka Children. Proc. Sri Lanka Ass. Adv. Sci (1989), 45, 20.

MAP OF SRI LANKA INDICATING JAPANESE ENCEPHALITIS ENDEMIC AREAS