REGIONAL COMMITTEE

Fifty-fifth Session
11-13 September 2002

Provisional Agenda item 10.2

SEA/RC55/7

25 July 2002

PREVENTION AND CONTROL OF DENGUE, JAPANESE ENCEPHALITIS AND KALA-AZAR IN SEA REGION

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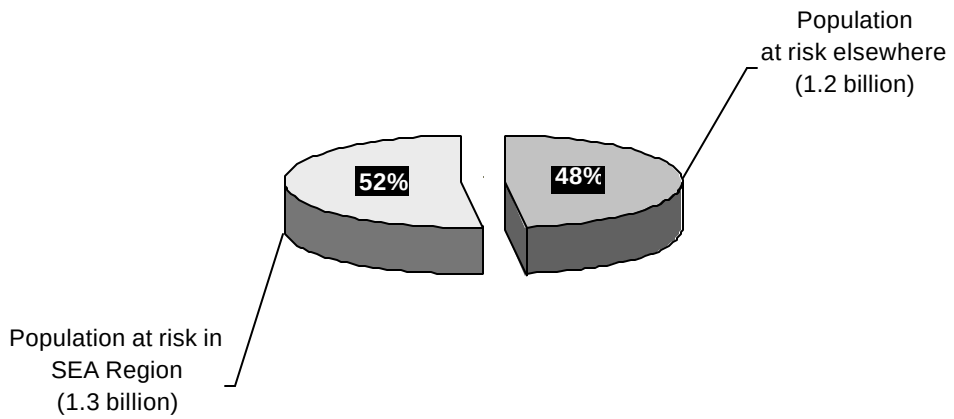
1. THE SITUATION

Dengue fever is an acute febrile viral disease caused by flaviviruses. There are four serotypes 1, 2, 3 and 4. The re-infections of these serotypes are responsible for dengue haemorrhagic fever (DHF) and the virus is transmitted to man by the bite of infective mosquitoes, mainly *Aedes aegypti*. This disease is now endemic in most of the tropical countries.

Dengue fever (DF), with its severe manifestations, such as dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS), has emerged as a major public health problem of international concern. It is a leading cause of childhood mortality in several Asian countries. Fifty two per cent of the population at risk of DF/DHF lives in the WHO South-East Asia Region (Figure 1). The geographical distribution has greatly expanded over the last 30 years because

Figure 1. *Population at risk of DF/DHF, 2001*



of increased potential for the breeding of *Aedes aegypti*.

Seven countries of the Region (Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka and Thailand) regularly report incidences of DF/DHF every year. Indonesia, Myanmar and Thailand fall in the tropical monsoon and equatorial climatic zone. The annual rainfall received by this region is less than 150 cm. There is widespread distribution of *Aedes aegypti* mosquito in both urban and rural areas. The transmission period is extended and DHF epidemics occur in 3-5 year cycles, associated with high morbidity in children. Bhutan and Nepal, being high altitude countries, have not reported any case of DF/DHF. DPR Korea, being a country with a temperate climate, has no report of indigenous transmission of DF/DHF.

The trend of reported cases of DF/DHF and deaths in the Region for the period 1985-2000 is shown in Figure 2. The total reported cases ranged from 46 458 in 1986 to 218 859 in 1998. During the epidemic years, the number of cases generally exceeds 100 000. Similarly, reported deaths due to DHF ranged from 2339 in 1987 to 471 in 1999. The

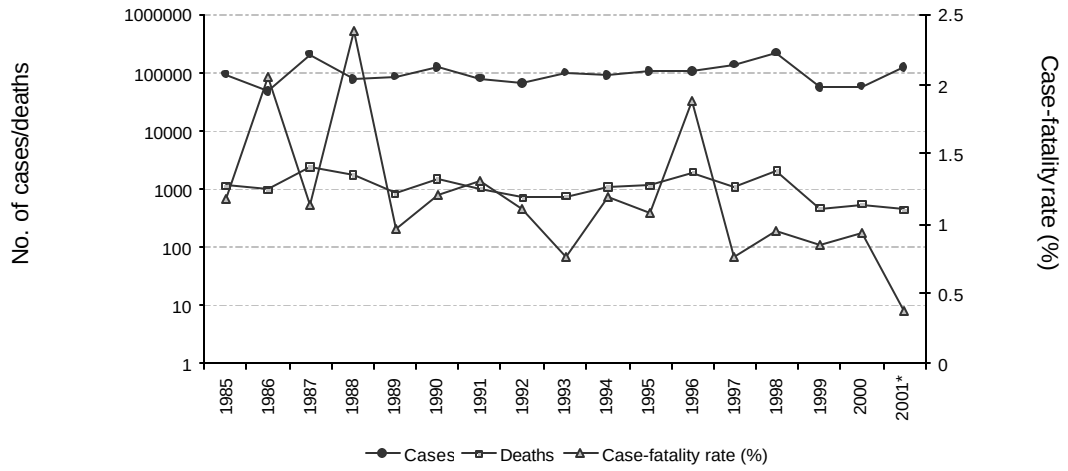
number of deaths due to DHF continues to be high (>1 000) in most of the years. The case-fatality rate, which fluctuated between 2 and 2.5 per cent up to 1990, has shown a downward trend; during 1997-98 it was stable and ranged between 1 and 2 per cent. Following the largest number of cases (218 859) reported in 1998, the number of reported cases declined markedly to 55 405 in 1999 and 57 997 in 2000. The number of deaths declined from 2 075 in 1998 to 471 in 1999 and 542 in 2000. However, the case-fatality rate remained around one per cent in 1999-2000.

Kala-azar or visceral leishmaniasis is a chronic and insidious disease caused by an intracellular protozoan (Leishmania species). It is a rural disease and man is the main reservoir of infection. Kala-azar is usually fatal if untreated. Sand fly (*Phlebotomus argentipes*), the vector of kala-azar, breeds in mud shelters located in peri-domestic and animal shelters. Poverty is a major determinant with the disease affecting the poor population who have little access to health facilities and cannot afford treatment.

Over 20% of the world's estimated 0.5 million annual cases occurred in the Indian states of Bihar, West Bengal and Uttar Pradesh. During 1999, a total of 12 728 kala-azar cases (284 deaths) were reported from India, of which 90% cases were detected in Bihar alone. Nepal reported kala-azar in areas along the border with Bihar and West Bengal, with 1 832 cases (28 deaths) in 1999. Bangladesh reported to 5 799 cases (24 deaths) in 1999.

Kala-azar has been recognized as a cross-border health problem affecting Bangladesh, India and Nepal. The incidence of kala-azar has a focus in the border districts, particularly on the India-Nepal border. There are sporadic cases in the Bangladesh-India border, but in Bangladesh the problem is more serious in areas far from the border.

Figure 2. *Number of reported cases of DF/DHF and deaths in the SEA Region* (1985-2001**)*



**** Bangladesh, India, Indonesia, Maldives, Myanmar, Sri Lanka and Thailand***

***** information upto September 2001***

Japanese encephalitis (JE) is a mosquito-borne zoonotic disease, caused by a group B arbovirus (flavivirus). It mainly infects animals and birds; Man is an incidental host. The disease usually occurs in areas under rice cultivation or with rich irrigation which favours the breeding of Culex mosquitoes. The risk increases in the presence of a large number of animal reservoir hosts such as pigs.

JE is a major public health problem in Asia and is the most important cause of viral encephalitis in the world. The most affected groups are children 1-15 years of age. JE affects rice-producing areas and is characterized by cyclic epidemics every two years.

JE is annually reported in four countries of the South-East Asia Region: India, Nepal, Sri Lanka and Thailand. Sporadic cases have also been reported in Indonesia and Myanmar. India and Nepal continue to report a high number of cases and deaths. The total number of cases reported in the Region in 1999 was 6 514 with 1 121 deaths. During the same period, India reported 3 428 cases with 680 deaths, Nepal 2 924 cases (434 deaths) while Sri Lanka and Thailand reported only 102 and 60 cases respectively with 3 and 4 deaths.

2. PREVENTION AND CONTROL

2.1 Regional Strategy for Prevention and Control of DF/DHF

The countries of the South-East Asia Region developed a regional strategy for the control of DF/DHF in 1995 which was revised in July 2001 with the following objectives:

(1) To establish an effective disease and vector surveillance system based on reliable laboratory and health information systems;

(2) To ensure early recognition and effective case management of DHF/DSS to prevent case mortality;

(3) To undertake disease prevention and control through integrated vector management with community and intersectoral participation;

(4) To undertake activities to achieve sustainable behavioural changes and partnerships;

(5) To establish emergency response capacity to control outbreaks with appropriate medical services, vector control, communications and logistics, and

(6) To strengthen regional and national capacities to undertake prevention and control of dengue and research related to epidemiology, disease and vector management and behavioural changes.

Each country formulated its national control programme according to its priorities, availability of infrastructure, resources, etc. Consequently, Thailand, Indonesia and Myanmar established National Dengue Prevention and Control Programmes while Sri Lanka has established a National Task Force for control of DF/DHF. India, Bangladesh and Maldives do not have National Dengue Control Programmes, but control is integrated as part of vector-borne disease control/malaria control organizations for emergency control of epidemics.

Surveillance is crucial for priority setting, policy decision to reduce disease burden, prediction and early detection of epidemics. All the countries of the Region have passive surveillance systems, which do not help in predicting epidemics.

Most of the dengue-endemic countries do not have the infrastructure to respond early and effectively to control epidemics. Emphasis is always on fogging and larvicide application. There has been an attempt to mobilize communities to undertake source reduction methods to prevent transmission. In most of the cases, the community will rely almost exclusively on government services to address the problem.

Prompt diagnosis and standardized treatment is a key to successful case management and thus reduce the case-fatality rate (CFR). In the SEA Region, clinicians and physicians in Thailand have provided the leadership in this direction. Seminal studies on the pathogenesis and pathophysiological changes in DHF patients were carried out in 1960 at Queen Sirikit's Institute of Child Health (WHO Collaborating Centre for Clinical Management of DF/DHF), which resulted in the development of guidelines for clinical diagnosis and management of severe cases to bring down CFR below 0.5%. These guidelines were adopted by WHO in 1975 and have also been incorporated into the IMCI (integrated management of childhood illness) protocols of Indonesia, Vietnam and the Philippines.

Based on the regional dengue control strategy of "selected, sustainable and integrated control approach with community and intersectoral participation", the countries of the Region have developed various models of community-based control programme based upon source reduction and have met with varying degree of success.

2.2 Strategy for Prevention and Control of Kala-azar

Kala-azar control is based on improving access for target population to early case detection and prompt treatment, vector control, health education as well as poverty alleviation measures. Kala-azar diagnosis is costly and unreliable. An antigen-based K-39 test has become available for rapid diagnosis. The anti-leishmaniasis drugs available for treatment are either unresponsive (1st line-SAG) or 2nd line drugs are very expensive (amphotericin B). These drugs are toxic and have to be administered parenterally for long periods. Increasing reports of resistant parasite against these drugs have become a major issue in control efforts. An oral drug, *miltefosine,* registered in India in early 2002, is under consideration for control programme in the India-Nepal border districts. Low coverage and periodic interruptions frequently hamper the vector control approach based on residual insecticide house spraying.

Experience in the past has shown that the incidence of kala-azar could be kept at a very low level for several years following large-scale interventions; the disease re-emerged when interventions could not be sustained. Thus, from the economic point of view, eradication of visceral leishmaniasis is not feasible, while control strategy would be too slow to contain the spread of the disease.

Kala-azar elimination

Objective

Progressive reduction of human reservoir until the disease is no longer a public health problem.

Target

By 2012, the annual incidence of kala-azar at the village level will not exceed 1 per 1000 population.

Time-frame

2003-2012

Strategy

- *Early detection:* Community awareness of the symptoms of kala-azar and when to seek treatment; surveillance and monitoring of drug resistance. Scaling up intervention targeting villages with a high burden of disease. Identification of individual cases using dipsticks followed by treatment with oral *miltefosine*. Use DOTS method to ensure compliance.
- *Prompt treatment in the nearest health facility:* Common protocol for diagnosis by using dipsticks, whenever possible, followed by treatment with oral *miltefosine*; community awareness on where to seek treatment and compliance.
- *Multi-disease approach and multi-pronged interventions:* Integrated care with other disease control such as malaria; promote wide use of insecticide-treated nets for community protection; environmental sanitation in and around the house; and integrated vector control. Application of two rounds of spraying with DDT for three consecutive years to quickly reduce vector density and curtail disease transmission.

- *Structured technical support:* Institutional support for technical networks for capacity building, Kala-azar cell in NAMP.
- *Operations research:* Establishment of indicators for monitoring progress of elimination; behavioural study for promotion of community action.
- *Coalition of stakeholders:* Government, civil society, private sector, international organizations, research institutions and foundations.

Implementation

- Programme will be implemented as part of cross-border collaboration under ICP- II 2002-2003 in four pilot districts, i.e. one each on the India-Nepal border and, similarly, one each on the Bangladesh-India border.
- Partnerships with industries to ensure the availability of cheap, reliable and sustainable supply of drugs, dipstick tests and insecticide for indoor residual spray.
- Development of a sensitive dipstick method for early detection of kala-azar.
- Production and marketing of affordable oral *miltefosine* as a drug of choice.
- Development of kala-azar vaccine, drug and diagnostic tools.

2.3 Strategy for Prevention and Control of Japanese Encephalitis

The strategy for prevention and control of JE includes three components: (1) Health education and training; (2) Vector control; (3) Immunization, and (4) Epidemic preparedness and response.

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.

Vector Control

Insecticide spraying is not considered as a major strategy. However, for the immediate suppression of infective vectors, ULV or thermal fogging may be employed, which again is not very cost-effective. Environmental measures are recommended.

Short-term measures

- Larviciding - impractical for widespread breeding habitats.

Long-term measures

- Water management, specially in irrigated rice fields, e.g. periodic drying of fields.
- Selection of rice varieties with minimum water requirements.
- Use of larvivorous fish.
- Environment manipulations like reduction of drainage, filling and weeding.

Immunization

- of population at risk i.e. children
- of pigs

Vaccination of humans is the only realistic tool to control JE. WHO recommends the use of JE vaccine wherever it is affordable. Suggestions have been made to incorporate the vaccine into EPI programmes in Asia.

Immunization of children

Since JE is annually reported in a few districts or pockets in the four JE endemic countries, e.g. on either side of the border between Nepal and India, immunization of children aged 6 months to 12 years is feasible. There are at least three vaccines being used: inactivated virus grown in mouse brain, inactivated virus grown on primary hamster kidney cells and live attenuated virus grown in primary hamster kidney cells (SA-14-14-2).

Vaccines have been used in Japan, Republic of Korea, Taiwan, China, Thailand and Nepal. A pilot study in Nepal found an eight-fold reduction compared with previous years and up to 88% of JE cases detected were found among unvaccinated people. China and Japan have successfully implemented vaccination with impressive results.

Pig vaccination

This is very costly, difficult and time-consuming. Pigs are normally slaughtered at 6-8 months of age. Vaccination must begin when maternal antibodies have decreased but before the pig becomes viraemic. Pig control has also been tried through segregation or slaughtering but this is difficult and the economic losses are high. Therefore, human vaccination is the most feasible and cost-effective tool for JE control.

Epidemic Preparedness and Response

(1) Immediately notify government authorities by phone, fax or email.

(2) A team of investigators consisting of clinicians, epidemiologists, entomologists etc. should be immediately sent to the affected site.

(3) The team should be provided 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

- CSF – for virus isolation and antibody tests
- in case of deaths – tissue samples of brain and liver.

All samples must be stored in a cool place. For virus isolation, samples must be stored at temperatures below –20°C.